Effects of Fasting on Glucagon-like peptide-1 hormone (GLP-1), and Lipid Profile Indices in Obese and Thin Women

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Abstract
Background
Glucagon-like peptide-1 hormone (GLP-1) contributes to the regulation of insulin and glucose concentration. However, the effects of fasting on GLP-1 response in different people has not been determined yet. The aim of the present research was to investigate the effect of fasting on GLP-1 and the lipid profile of obese and thin women.

Materials and Methods: In this research, 25 obese and thin women whose age ranged from 35 to 45 years were selected through a convenient sampling method and were divided into two groups of obese (n=12, body mass index >30 kg/m2) and thin (n=13, body mass index=18-20 kg/m2). GLP-1 in both groups was measured in four phases: 3 days before the beginning of Ramadan, 14 days after the beginning of Ramadan, 28 days after the beginning of Ramadan and 2 weeks after the end of Ramadan. Repeated–measure ANOVA was used to statistically analyse the data.

Results
GLP-1 was reduced from phase 1 to 3 of the research. However, it was increased after Ramadan. In the thin group, GLP-1 was increased in 14 days of fasting, but did not show any change at the end of Ramadan, and also two weeks after this month. However, none of these changes were statistically significant. The two groups did not diverge from each other significantly in any of the phases.

Conclusion
The present findings showed that fasting has no significant effect on the GLP-1 and lipid profile indices of the obese and thin women.

Key Words: Fasting, Glucagon-like peptide-1 hormone, Obese, Women.

1- INTRODUCTION

In recent years, the hormones involved in adjusting energy in intestines have been discovered one of which is the Glucagon-like peptide-1 hormone (GLP-1). It has shown to inhibit food absorption and weight gain (1). This peptide is known as a type of incretin. Incretins are a group of metabolic hormones secreted in response to glucose consumption by intestinal cells and play a key role in glucose homeostasis (2). Moreover, these hormones account for the secretion of 50-70% of the insulin secreted upon consuming oral glucose (3).

GLP-1, on the one hand, directly increases the gene expression of insulin and its synthesis through the existing receptors on pancreas cells (4), and on the other hand, directly affects its own receptors and pancreas beta cells indirectly through the vagus nerve and hepatic portal vein and increases insulin secretion and decreases blood glucose (5). Upon entering the portal blood stream, GLP-1 activates a glucose sensor in the portal vein which sends signals to the central nervous system and the brain through vagus nerves and then again through vagus nerves sends signals to the pancreas which increases the secretion of insulin in pancreas. It also directly affects pancreas alpha cells and reduces the secretion and release of glucagon (5). Moreover, GLP-1 reduces the speed of stomach evacuation and causes a slow absorption and prevents the sudden increase of blood glucose. It creates a feeling of satiation and thus cuts down on food consumption (6).

Moreover, GLP-1 can independently improve the accumulation of hepatic glycogen, increase glucose absorption and decrease the concentration of triglycerides (7). A particular nutritional condition facing all Muslims worldwide on a yearly scale is fasting in Ramadan. The procedure involves refraining from eating, drinking and smoking from the out set of sunrise up until sunset. They are allowed to consume foods and drinks in the time between sunset and the next sunrise. In other words, the regular meal pattern would change to two meals a day in Ramadan (8), which can contribute to the diet plan of inactive obese individuals and improve their lipid profile. How fasting affects blood biochemical indices is not determined yet and is under investigation. Fasting in Ramadan is a perfect opportunity for correcting one’s diet and can affect fasting blood sugar (FBS), insulin concentration, insulin resistance, total cholesterol (TC), triglyceride (TG), Low-density lipoprotein (LDL-C), High-density lipoprotein (HDL-C), and proportion of total cholesterol to high-density lipoprotein (TC/HDL-C), and proportion of low-density lipoprotein to high-density lipoprotein (LDL-C/HDL-C). There have been contradictory research findings on how fasting affects blood fats in healthy individuals with no extra weight (8-11). The role GLP-1 plays in obesity pathogenesis is not clarified yet.

In obesity, GLP-1 level and insulin level have been suggested to correlate negatively. That is to say that resistance to insulin may cause a weak GLP-1 response and lead to the gain of more weight (12). The reaction of GLP-1 to one meal after a long-term loss of weight and after fasting is not known yet. Only a few investigations looked into the acute effect of the weight lost in response to a diet on the basic and fasting levels of GLP-1.

Verdict et al. (2001) indicated the poor response of fasting GLP-1 in obese subjects which was significantly increased after a six-month weight loss through a diet. There seems to be mediating factor involved between GLP-1 response in thin and obese people and this mediating factor is GLP-1 response to weight loss (12). A body of research reported a lower plasma level of fasting GLP-1 and lower Glp-1 response to food consumption in obese individuals (13-15). Some other research reported an increased GLP-1 response to
consuming food stuff in obese human and rats (16). As for the loss of weight, other investigations that involved a weight loss intervention reported the reduction (17-19), and no change (20) of GLP-1 level after the weight loss through a diet. Yet, the effect of fasting on GLP-1, and lipid profile values in thin and obese people is not determined and requires further investigation. Thus, the present research aimed to investigate the effect of fasting on the GLP-1 and lipid profile of thin and obese women.

2- MATERIALS AND METHODS

The research methodology followed in this study was semi-experimental with repeated measures and two case groups. The sample was comprised of women from Mashhad city, Iran. Among those who met the inclusion criteria, 25 women whose age ranged between 21 and 51 years, and formerly filled out the written consent form were selected through convenient sampling method. They were divided into two groups of obese (n=12, body mass index [BMI] >30 kg/m2), and thin (n=13, BMI=18-20 kg/m2). These subjects were diagnosed as healthy according to a demographic information questionnaire, and their medical record.

They had no experience of smoking, cardio-vascular, renal, respiratory, hepatic and metabolic diseases. The study was conducted in Ramadan (2017), and it lasted for seven weeks (one week before until two weeks after the end of Ramadan). It is noteworthy that due to the long-term fasting, voluntary participation in the study, considering the ethical issues and continuous attention to people’s health, one subject was excluded from the thin, and one from the obese group as they did not meet the research conditions (travel, absence for more than three sessions of exercise and omission of the Sahar meal) during the research procedures. Their previous information was omitted too.

Therefore, the thin group ended up with 12 and the obese group with 11 subjects examined in four phases (3 days before Ramadan, 14 days after the beginning of Ramadan, the end of Ramadan and 14 days after Ramadan). The anthropometrics used in this research included: standing height (Seca stadiometer made in Germany, precision of 5 mm), weight (Seca scale, precision of 100 gr), body composition (impedance bioelectrical scale, Inbody 720, made in South Korea).

All these measurements were done in the morning time. The subjects were formerly asked to avoid intensive physical activities two days before the test. The measurement was to be done when the subjects’ bladder, bowels and stomach were emptied. All the tests were given from 1:00 p.m. to 2:30 p.m. Moreover, in the present research, 7ml blood samples were taken from median cubital vein from 4:00 to 6:00 p.m. after at least 12 hours of fasting in Dr. Sezavar’s medical diagnostic lab.

The serum of these samples was immediately centrifuged. Then an automatic analyzer as well as Pars-Azmoon kits were used to measure HDL, TG, TC, and LDL. GLP-1 was measured by GDV-ELISA Reader. Once the data were collected, they entered SPSS software version 24.0 for the required statistical analysis. The data were appropriately labeled and analyzed through descriptive and inferential statistics.

The former included mean scores, distribution indices and plots. The latter involved exploratory Shapiro-Wilk and Levene tests which examined the normality of data and homogeneity of group variances, respectively. Repeated-measure ANOVA was used to compare within-group and inter-group mean scores. To make statistical decisions, the significance level was set at p<0.05.
3- RESULTS

The mean and standard deviation of obese subjects’ age was 44.5±4.9 years, while that of the thin group was 30.84±8.99 years. According to Table.1, within-group variation in the means cores of weight, BMI and body fat were not statistically significant in either group (p>0.05). Only the between-group proportion of waist circumference to hip circumference and the percentage of fat were significantly different (p<0.05).

The results presented in Table.2 indicate significant within-group changes in total cholesterol, low-density lipoprotein and high-density lipoprotein in the obese group and only high-density lipoprotein in the thin group (p<0.05). Within-group variation in the mean scores of GLP-1 and triglyceride was not statistically significant in either group. Similarly, the within-group variation in total cholesterol and low-density lipoprotein was not statistically significant in the thin group (p>0.05).

### Table 1: Within- and between-group anthropometric differences in the thin (n=12), and obese (n=11) groups

<table>
<thead>
<tr>
<th>Anthropometric measure</th>
<th>Group</th>
<th>Phases</th>
<th>Within-group variation</th>
<th>Between-group variation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>3 days before Ramadan</td>
<td>2nd week of Ramadan</td>
<td>4th week of Ramadan</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>Obese</td>
<td>82.88±8.6</td>
<td>82.13±8.62</td>
<td>82.23±9.03</td>
</tr>
<tr>
<td></td>
<td>Thin</td>
<td>53.53±5.91</td>
<td>53.16±5.72</td>
<td>53.50±5.63</td>
</tr>
<tr>
<td>BMI (kg/m2)</td>
<td>Obese</td>
<td>33.62±3.43</td>
<td>33.36±3.53</td>
<td>33.39±3.62</td>
</tr>
<tr>
<td></td>
<td>Thin</td>
<td>20.31±1.32</td>
<td>20.17±1.28</td>
<td>20.30±1.30</td>
</tr>
<tr>
<td>Waist /hip circumference (cm)</td>
<td>Obese</td>
<td>1.01±.06</td>
<td>.9±.08</td>
<td>1.0±.07</td>
</tr>
<tr>
<td></td>
<td>Thin</td>
<td>.81±.03</td>
<td>.80±.03</td>
<td>.81±.03</td>
</tr>
<tr>
<td>Body fat (%)</td>
<td>Obese</td>
<td>45.43±5.27</td>
<td>44.89±5.68</td>
<td>45.05±5.04</td>
</tr>
<tr>
<td></td>
<td>Thin</td>
<td>30.40±5.61</td>
<td>30.51±5.51</td>
<td>30.47±5.49</td>
</tr>
</tbody>
</table>

BMI: Body mass index.

Bonferroni post-hoc test results showed statistically significant within-group variation (in the thin group) in the mean scores of waist /hip circumference between the 2nd phase (2nd week of Ramadan) and the fourth phase (2 weeks after Ramadan), high density lipoprotein between the 2nd phase (2nd week of Ramadan) and the third phase (4th week of Ramadan), and also between the second phase (2nd week of Ramadan), and the fourth phase (2 weeks after Ramadan). In the obese group, within group variances revealed significant changes in the mean scores of high-density lipoprotein between the first phase (3 days before Ramadan) and the second phase (2nd week of Ramadan), in the low-density lipoprotein between the first phase (3 days before Ramadan) and the fourth phase (2 weeks after Ramadan), and in the total cholesterol between the second phase (2nd week of Ramadan), and the fourth phase (2 weeks after Ramadan). According to the results presented in Table.2, variation in within-group means cores was not statistically significant in any of the target variables in either group (p>0.05).
Table-2: Within- and between-group biochemical differences in the thin (n=12), and obese (n=11) groups

<table>
<thead>
<tr>
<th>Biochemical measure</th>
<th>Group</th>
<th>Phases</th>
<th>Within-group variation</th>
<th>Between-group variation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>3 days before Ramadan</td>
<td>2nd week of Ramadan</td>
<td>4th week of Ramadan</td>
</tr>
<tr>
<td>GLP-1</td>
<td>Obese</td>
<td>185.06±185.85</td>
<td>179.46±189.35</td>
<td>166.66±109.03</td>
</tr>
<tr>
<td></td>
<td>Thin</td>
<td>278.07±252.73</td>
<td>310.85±250.22</td>
<td>295.74±277.79</td>
</tr>
<tr>
<td>TG (mg/dl)</td>
<td>Obese</td>
<td>126.22±41.09</td>
<td>127.81±26.70</td>
<td>125.±43.85</td>
</tr>
<tr>
<td></td>
<td>Thin</td>
<td>113.23±40.48</td>
<td>107.07±38.52</td>
<td>105.46±35.67</td>
</tr>
<tr>
<td>TC (mg/dl)</td>
<td>Obese</td>
<td>207.41±32.87</td>
<td>216.75±28.45</td>
<td>201.72±35.19</td>
</tr>
<tr>
<td></td>
<td>Thin</td>
<td>178.46±37.31</td>
<td>184.07±36.14</td>
<td>173.61±32.33</td>
</tr>
<tr>
<td>LDL (mg/dl)</td>
<td>Obese</td>
<td>121.68±26.24</td>
<td>113.36±19.97</td>
<td>105.27±25.32</td>
</tr>
<tr>
<td></td>
<td>Thin</td>
<td>98.53±26.93</td>
<td>94.69±24.31</td>
<td>92.46±23.09</td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td>Obese</td>
<td>51.12±6.85</td>
<td>61.66±9.56</td>
<td>52.90±8.97</td>
</tr>
<tr>
<td></td>
<td>Thin</td>
<td>51.34±8.84</td>
<td>58.07±6.73</td>
<td>50.38±10.03</td>
</tr>
</tbody>
</table>

GLP-1: Glucagon-like peptide-1; TG: triglyceride; TC: total cholesterol; LDL: low density lipoprotein; HDL: high density lipoprotein.

**4- DISCUSSION**

The present research aimed to investigate the effect of fasting on the GLP-1 and lipid profile of thin and obese women. The results showed that in neither group (thin or obese), fasting had any significant effect on GLP-1. In some other research, it was found that the thin and obese groups diverged significantly in terms of GLP-1 catabolism. This difference was associated with the activity of IV dipeptide peptidase (15). However, in the present research, the thin and obese groups did not diverge from each other in terms of GLP-1 changes. Quite many investigations (21-27) reported an increase in incretin after the stomach bypass surgery. It is not yet determined whether calorie deficiency or rapid weight loss are involved in the change of incretin level since the weight loss induced by a diet is correlated with high GLP-1 level (even to a limited degree) (12). GLP-1 has been observed to be increased significantly in response to oral glucose one month after the bypass surgery (28). GLP-1 level tends to be reduced after a nutritional diet thought not to a significant degree. This finding is in contrast with what Verdich et al. found in terms of the increased GLP-1 level (even to some degree) during one meal after loss of weight among men (12). The time spent after the surgery which has differed from one research to the other can be a key variable as a body of research has shown that increased GLP-1 is temporary and does not continue in 6-12 months of surgery (29). The effect of fasting in Ramadan was observed in the present research more on the lipid indices of obese subjects than the thin. This difference can be probably explained by higher basic levels of TG, TC, and LDL of the obese group than the thin. With this respect,
some other research with 96 subjects afflicted with hyperlipidemia who received consultation on correcting their lifestyle reported that the effect size of controlling diet on TC and LDL levels is correlated with their basic levels (30). Therefore, the lower basic level in the thin group might have limited the effect size of fasting on lipid indices in this group. How fasting in Ramadan affects blood biochemical indices is not determined yet. Overall, fasting in Ramadan is a good opportunity for correcting one’s nutritional diet and can affect LDL, TG, TC and HDL. Moreover, there have been contradictory findings concerning the effect of fasting on the lipids of healthy people.

TC is among the key biochemical indices and includes a certain category of lipids which, if exceeds a natural range, is accompanied by the risk of artherosclerosis. Therefore, examining its variation profile during fasting in Ramadan is of a great significance. According to a body of existing research, Haghdooost and Poorranjbar (2009), and Yarahmadi et al. (2003) reported an increase in TC during Ramadan (10, 31). On the contrary, Boobes et al. (2009), and Mansi (2007) reported the reduction of TC (9, 32). Lipoproteins rich in cholesterol such as LDL may be increased during Ramadan. However, several researchers proved to the contrary (33-35). Recent findings attested to the lacking variation in HDL concentration during Ramadan. Some others, yet found a significant increase in HDL concentration (33-36).

Changes in blood lipid level can be correlated with the amount of food consumed among those who eat excessively during the day (37). Lower energy consumption in Ramadan is correlated with lower TC and plasma LDL that act as cardiovascular factors (38, 39). Nevertheless, contradictory findings can be explained by the fact that Ramadan follows a lunar calendar rather than a solar calendar cycle. Therefore, the duration of fasting limited to the hours of day differ across countries and varies across years. It depends on whether the fasting is done during hot and long summer days or in short and cold winter days. Moreover, ethnic/national differences as well as socioeconomic differences can be involved that affect nutritional diets. These factors can tremendously affect the measured variables in different studies conducted in previous years.

4-1. Limitations of the study

One limitation of the present study is the absence of a control group as it was impossible to find healthy subjects not fasting in Ramadan. Another limitation was that the subjects’ nutritional diet was not controlled and they could eat freely at night. Moreover, the target research population was 25 subjects which made it rather insufficient for the required statistical analyses.

5- CONCLUSION

According to the results, variation (GLP-1, and lipid profile) in within-group means cores was not statistically significant in any of the target variables in obese and thin groups. The present findings showed that fasting has no significant effect on the GLP-1 and lipid profile indices of the obese and thin women.

6- CONFLICT OF INTEREST: None.

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