Effects of 12-week high-intensity interval training on plasma visfatin concentration and insulin resistance in overweight men

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Abstract

The purpose of this study was to determine the effects of 12 weeks of high-intensity interval training (HIIT) on visfatin and insulin resistance (IR) in overweight adult men during a weight-loss program. Eighteen overweight men (age = 31.8 ± 9.2 years; body mass index = 28.6 ± 1.4 kg/m²) were randomly recruited into one of the two groups, namely, HIIT (3 days/week, 20 minutes/day; 85–95% peak oxygen uptake) and diet-induced weight-loss combined (DHIIT; n = 10) and diet-induced weight loss only (DIO; n = 8). The DHIIT and DIO groups undertook a 12-week weight-loss intervention using a moderate isocaloric energy-deficit diet. Both DHIIT and DIO groups demonstrated a significant reduction in body weight (p < 0.01). Total fat mass (p < 0.05) and lean body mass (p < 0.05) were decreased in the DIO group with no significant changes in abdominal fat mass, plasma insulin concentration, homeostasis model assessment-estimated IR (HOMA-IR), blood glucose level, and plasma visfatin. In the DHIIT group, total fat mass (p < 0.01), abdominal fat mass (p < 0.05), plasma insulin concentration (p < 0.05), plasma visfatin (p < 0.01), and HOMA-IR (p < 0.05) were reduced and lean body mass remained unchanged. In conclusion, adding a low-volume 20-minute HIIT (three times/week) to an energy-deficit diet not only can improve the efficiency of weight-loss program in the reduction of body fat, plasma visfatin levels, and HOMA-IR, but also has a reservation effect on lean body mass.

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Keywords: High-intensity interval training; Homeostasis model assessment-estimated insulin resistance; Visfatin; Weight loss

Introduction

Visfatin is a new obesity-related adipokine that is isolated from the visceral adipose tissue. However, some subsequent studies were unable to find differences in visfatin messenger RNA expression between visceral and subcutaneous adipose tissues in humans. There are conflicting results regarding the changes in plasma visfatin levels during the development of obesity, with some reporting an increase and some reporting a decrease in levels. It is primarily supposed that visfatin exerts an insulin-mimetic effect by binding to and stimulating the insulin receptor as well as by lowering plasma glucose levels. Nevertheless, several studies have revealed a negative association between plasma visfatin level and insulin sensitivity. According to Haider et al, hyperglycemia enhanced circulating visfatin levels in humans, suggesting that visfatin release may be associated with plasma glucose concentration. Finally, some studies suggest that visfatin may be involved in a mechanism that induces insulin secretion in isolated pancreatic islets.
circulating serum concentrations of visfatin in obese individuals (e.g., Manco et al\textsuperscript{8} Haider et al\textsuperscript{9} De Luis et al\textsuperscript{10}); by contrast, a previous study reported that weight loss after gastroplastic surgery is associated with an increase in circulating concentrations of visfatin, which correlated with the decrease in insulin resistance (IR).\textsuperscript{11} De Luis et al\textsuperscript{12} in a study conducted on morbidly obese patients, found out that weight reduction after a hypocaloric diet is not accompanied by a change in circulating visfatin levels; however, fat mass, fat-free mass, serum glucose, insulin, and homeostasis model assessment (HOMA) decreased. Agueda et al\textsuperscript{13} findings demonstrated that lean mass changes due to weight loss might be more effective than fat mass changes in serum visfatin concentration. Only limited studies that reported the effects of exercise on circulating visfatin are available. Several studies suggest that exercise training with weight loss induces reduction of plasma visfatin concentration that is accompanied by benefits to body composition, metabolic syndrome factors, and IR.\textsuperscript{14–16} Nevertheless, Seo et al\textsuperscript{17} did not find any changes in plasma visfatin levels after combined exercise training in healthy women.

Most recent studies have examined the effects of aerobic exercise training or a combination of resistance training and aerobic exercise training on plasma visfatin level, IR, and body composition in overweight or obese individuals.\textsuperscript{14–17} Increasing evidence suggests that high-intensity interval training (HIIT) through positive changes in hormone secretion and enzymatic adaptation can effectively improve abdominal and subcutaneous fat loss, IR, fat oxidation, appetite regulation, and aerobic capacity.\textsuperscript{18–20} In addition, HIIT involves noticeably lesser training volume, making it a time-efficient approach with increased health benefits compared with aerobic exercise training.\textsuperscript{21,22} Consequently, it is possible that visfatin would respond to low-volume HIIT. To the best of our knowledge, there is no study that has investigated the effects of HIIT on circulating visfatin in overweight and obese men during the weight-loss program. Thus, the purpose of our study is to define the effects of 12 weeks of HIIT on visfatin and IR in overweight and obese adult men during a weight-loss program.

Methods

Participants

A total of 18 healthy men (age = 31.8 ± 9.2 years) were recruited for this study. The participants had been registered for a weight-loss program by Iranian Health Clinic of Isfahan, Iran. All participants underwent a complete medical examination, filled up the physical activity questionnaire, and had their weight and height measured before inclusion. We omitted the participants who were smokers, had any severe illness (e.g., diabetes, cardiovascular disease), or were taking medication that could affect laboratory test results. All participants were overweight [body mass index (BMI) = 28.6 ± 1.4 kg/m\textsuperscript{2}] with a sedentary lifestyle (less than 20-minute exercise two times/week). Participants were randomly assigned to either an HIIT and diet-induced weight-loss combined (i.e., DHIIT; n = 10) or diet-induced weight loss only (DIO; n = 8) group. For each participant, both pretests and post-tests were executed at the same time of the day. There was no significant difference between the two groups with respect to age, weight, height, or BMI. The Sport Science Department of the Central Branch of Tehran Azad University approved the study protocol. The participants signed an informed consent document before participation.

Training program

Each high-intensity interval exercise session involved repeated 60-second running at a high intensity (85–95% heart rate reserve), which was alternated by 60-second running at a low intensity (55–60% heart rate reserve) for recovery.\textsuperscript{23} Participants finished six high-intensity intervals during the 1st week, eight intervals during the 2nd week, 10 intervals during the 3rd–8th weeks, and 12 intervals on the final 4 weeks. A 5-minute low-intensity running was performed as a warm up in the beginning and 3-minute recovery period was provided at the end of each training session. Therefore, each main exercise lasted between 20 and 24 minutes approximately. The total training program was carried out for 12 weeks, three times/week (Saturday, Monday, and Wednesday) under the supervision of an exercise physiologist. To assess the peak oxygen uptake (VO\textsubscript{2peak}), all participants performed an incremental graded exercise test to exhaustion (Balk protocol) on a programmable treadmill, while using an online gas analyzer system (PowerCube, GANSHORN, Germany). To indicate the attainment of VO\textsubscript{2peak}, the following criteria were fulfilled: oxygen uptake plateaus with a further increase in workload, a respiratory exchange ratio (RER) more than 1.15, ratings of perceived exertion (RPE) more than 17, volitional exhaustion, and an heart rate (HR) greater than or equal to age-predicted maximum. The energy expenditure of each exercise session totaled to about 300–400 kcal that was calculated by the VO\textsubscript{2} consumption corresponding of heart rate during exercise.\textsuperscript{24} All participants used a heart rate monitor device during every exercise session to control the targeted heart rate.

Dietary intervention

Daily caloric requirements were predicted using body weight, height, age, gender, and physical activity level. The weight-loss diet consisted of an energy-deficit diet by 2000–3000 kcal/week in the DHIIT group and 3000–4000 kcal/week in the DIO group. The dietary protocol was a balanced healthy diet that included the six categories of foods. The balanced diet comprised 50–55% carbohydrate, 20–25% protein, and 25–30% fat. All participants visited the nutritionist once a week to assess their dietary intake, obtain dietary recommendations, and calculating reduction in weight.

Body composition

Body composition was measured using a dual-energy X-ray absorptiometry (DEXA) scanning device (Discovery-A,
Blood samples were taken in the morning after an 8–9-hour overnight fasting. Blood samples were centrifuged for 10 minutes at 4°C and plasma samples were stored at −80°C for subsequent analyses. Blood samples were collected 3 days before the start of the training program and 48 hours after the last exercise session. Plasma visfatin levels were measured using a specific enzyme-linked immunosorbent assay (ELISA) kit (Phoenix Peptides, Karlsruhe, Germany). The intra-assay coefficient of variation (CV) was approximately 5%. Human insulin ELISA kit was used to measure the plasma insulin concentration (DiaMetra, Foligno, Perugia, Italy) with an intra-assay CV less than 4.5%. The glucose oxidase technique was used to measure blood glucose levels. The IR was calculated by the HOMA for all participants. The HOMA-IR was used to measure blood glucose levels. The IR was calculated using the formula \([\text{fasting glucose (mmol/L)}]/[\text{insulin (mU/mL)}]/22.5]\).25 A single assessor took all samples in duplicate for each factor.

Statistical analyses

Descriptive data were expressed as means ± standard deviations. Differences between the DIO and DHIIT group characteristics were verified by independent Student \(t\) test at baseline. Changes in variables from pretest to post-test were detected by paired Student \(t\) test. The two-way repeated measures analysis of variance method was applied to measure group–time interactions (group × time; 2 × 2). Statistical significance was set at \(p < 0.05\) and SPSS 15.0 was used for all analyses (SPSS Inc., Chicago, IL, USA).

Results

Table 1 shows all characteristics at baseline. There were no significant differences between the two groups on any parameter before intervention (Table 1).

Body weight reduction after the 12-week intervention in the DIO group was 5.4% (5.0 ± 1.6 kg; \(p < 0.01\)) and in the DHIIT group it was 8% (7.2 ± 2.6 kg; \(p < 0.01\)). In the DIO group, significant decreases were observed in fat mass (\(p < 0.05\)) and lean body mass (\(p < 0.05\)). However, there was no significant change in blood glucose level, abdominal fat mass, plasma insulin concentration, HOMA-IR, and plasma visfatin. In the DHIIT group, we found significant reduction in fat mass (\(p < 0.01\)), abdominal fat mass (\(p < 0.05\)), plasma insulin concentration (\(p < 0.05\)), plasma visfatin (\(p < 0.01\)), and HOMA-IR (\(p < 0.05\)), while no significant variation in total lean mass and blood glucose level was observed in this group (Table 2).

A significant group–time interaction was observed for some parameters. In comparison with the DIO group, the DHIIT group had greater decreases in total fat mass (\(p < 0.05\)) and abdominal fat mass (\(p < 0.05\)). However, there was no significant group–time interaction in body weight, plasma insulin concentration, blood glucose level, HOMA-IR, plasma visfatin levels, and total lean body mass (Table 2).

Discussion

The results of this study indicate that both DHIIT and DIO significantly decreased body weight, but only DHIIT caused a significant reduction in plasma visfatin level, abdominal fat mass, fasting insulin level, and HOMA-IR. Although both weight-loss programs decreased total fat mass, the reduction was significantly more in DHIIT than in DIO. There was a significant loss of total lean mass only in the DIO group.

Both DHIIT and DIO protocols decreased body weight by 8% and 5.4%, respectively. Body weight reduction was greater (but not significant) in the DHIIT compared with the DIO group; however, the total energy deficit was the same in the both groups. The difference in weight loss may be explained by the fact that high-intensity exercise increases metabolic rate and decreases energy intake in the postexercise state.26,27 Interestingly, weight loss in the DHIIT group is accompanied by a major reduction in fat mass and almost no change in lean mass, whereas in the DIO group, considerable fraction (40%) of weight loss was due to lean mass reduction. These findings are in agreement with those reported by Tremblay et al21 and Trapp et al.22 Elevated catecholamine levels in response to HIIT can explain major reduction of fat mass in the DHIIT group as catecholamine would stimulate lipolysis.

### Table 1

<table>
<thead>
<tr>
<th>Parameter</th>
<th>DHIT ((n = 10))</th>
<th>DIO ((n = 8))</th>
<th>(p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>31.4 ± 10.2</td>
<td>32.5 ± 9.3</td>
<td>0.87</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>176.0 ± 7.5</td>
<td>182.2 ± 4.9</td>
<td>0.19</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>90.6 ± 8.9</td>
<td>92.7 ± 7.0</td>
<td>0.70</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>29.2 ± 1.6</td>
<td>28.1 ± 0.7</td>
<td>0.19</td>
</tr>
<tr>
<td>Fat mass (kg)</td>
<td>34.9 ± 3.6</td>
<td>34.8 ± 3.4</td>
<td>0.99</td>
</tr>
<tr>
<td>Abdominal fat mass (kg)</td>
<td>4.7 ± 0.6</td>
<td>4.5 ± 1.0</td>
<td>0.71</td>
</tr>
<tr>
<td>Lean body mass (kg)</td>
<td>53.3 ± 5.6</td>
<td>55.5 ± 0.9</td>
<td>0.49</td>
</tr>
<tr>
<td>Glucose (mmol/L)</td>
<td>4.7 ± 0.3</td>
<td>4.6 ± 0.5</td>
<td>0.72</td>
</tr>
<tr>
<td>Insulin (µU/mL)</td>
<td>8.0 ± 1.8</td>
<td>11.0 ± 4.1</td>
<td>0.19</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>1.6 ± 0.3</td>
<td>2.2 ± 0.8</td>
<td>0.24</td>
</tr>
<tr>
<td>Visfatin (ng/mL)</td>
<td>16.2 ± 3.5</td>
<td>19.2 ± 2.7</td>
<td>0.20</td>
</tr>
</tbody>
</table>

Data are presented as mean ± standard deviation.

BMI = body mass index; DHIT = diet and high-intensity interval training combined; DIO = diet-induced only; HOMA-IR = homeostasis model assessment-estimated insulin resistance.
that is largely responsible for fat release from adipose tissue fat stores.\textsuperscript{28,29} The anabolic effects of growth hormone (GH) have been demonstrated extensively.\textsuperscript{30} Thus, a marked elevation in plasma GH after a high-intensity exercise bout that continues to be high even after 1 hour following an exercise\textsuperscript{31,32} could be an explanation for lean mass retention in the DHIIT group. Overall, these data show that addition of HIIT (3 sessions/week) to a weight-loss program results in a significant improvement in weight loss, fat mass reduction, and lean mass maintenance.

An important finding of this study was that plasma visfatin did not significantly change in the DIO group. Changeless visfatin levels seen in this group is consistent with that reported by De Luis et al\textsuperscript{12} who reported that a moderate hypocaloric diet in morbidly obese individuals, despite a significant reduction in weight (4.4%), fat mass, fat-free mass, and HOMA was not accompanied by a change in circulating visfatin. However, our findings do not support the results of De Luis and co-workers' study,\textsuperscript{10} in that they found that weight loss after 12 weeks of hypocaloric diet is related to significant decreases in plasma visfatin level in obese individuals. One possible explanation for this discrepancy is that body weight reduction in the DIO group of this study is not sufficient for a significant reduction in circulating visfatin.

This is the first study to survey the effects of HIIT program on plasma visfatin concentration in sedentary, adult, overweight, or obese men during a weight-loss program. Significant reduction in the plasma visfatin level in the DHIIT group was the main finding of this study. This finding has also been observed in previous studies that used endurance or combined exercise training (e.g., Choi et al\textsuperscript{14} Seo et al\textsuperscript{15} Haus et al\textsuperscript{16}). Seo et al\textsuperscript{15} showed that 12 weeks of combined (aerobic and resistance) exercise training lowered plasma visfatin concentration in obese women that was accompanied by positive changes in body composition. Choi et al\textsuperscript{14} have also executed a combined training program on Korean healthy women that included aerobic training (45 minutes/session) and strength training (20 minutes/session) five times/week for 3 months. They found significant decreases in visfatin levels and body weight of participants. Besides, Haus et al\textsuperscript{16} found that incremental aerobic exercise training also resulted in significant reduction in plasma visfatin in addition to weight loss and body composition changes. However, Seo et al\textsuperscript{17} did not find any significant changes in visfatin level despite significant reduction in body weight and fat percentage. These findings show that low-volume HIIT (60 minute/week) has the same effects as high volume combined or aerobic exercise training (180—300 minute/week) on visfatin levels.

The present study revealed that DHIIT, but not DIO, significantly decreased plasma visfatin levels. This difference may be due to increased reduction of total and abdominal fat mass in the DHIIT group. It is based on the suggestion that visceral adipose tissue is the main site of visfatin production.\textsuperscript{1} Moreover, Haus et al\textsuperscript{16} have demonstrated a strong correlation between alteration in visfatin levels and visceral adipose tissue. Further, some studies have shown a significant reduction in body fat mass along with reduction in plasma visfatin level.\textsuperscript{6,9} The other possible explanation for this difference is a significant reduction of lean mass in the DIO group. This has been supported by the results of Agueda et al\textsuperscript{13} who demonstrated that changes in lean mass due to weight loss might be more effective than fat mass changes in serum visfatin concentration. They found a significant negative association between the change in plasma visfatin and the change in lean mass, without any relationship between fat mass and visfatin changes after energy-restricted diet intervention.

Finally, we found that fasting plasma insulin concentration and HOMA-IR were significantly reduced in the DHIIT group, whereas there was no significant change in the DIO group. The high effectiveness of HIIT on HOMA-IR reduction has been observed in previous studies.\textsuperscript{22} The significant decrease of HOMA-IR in the DHIIT group can be due to the reduction in abdominal fat mass. This is in line with significant association

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**Table 2**

<table>
<thead>
<tr>
<th></th>
<th>Pre</th>
<th>Post</th>
<th>p</th>
<th>Pre</th>
<th>Post</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (y)</strong></td>
<td>31.4±10.2</td>
<td>-</td>
<td>-</td>
<td>32.5±9.3</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Height (cm)</strong></td>
<td>176.0±7.5</td>
<td>-</td>
<td>-</td>
<td>182.2±4.9</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Body weight (kg)</strong></td>
<td>90.6±8.9</td>
<td>83.4±9.7</td>
<td>0.004*</td>
<td>92.7±7.0</td>
<td>87.7±7.3</td>
<td>0.009**</td>
</tr>
<tr>
<td><strong>BMI (kg/m²)</strong></td>
<td>29.2±1.6</td>
<td>26.8±2.1</td>
<td>0.004*</td>
<td>28.1±0.7</td>
<td>26.3±0.7</td>
<td>0.011***</td>
</tr>
<tr>
<td><strong>Fat mass (kg)</strong></td>
<td>34.9±3.6</td>
<td>28.6±4.6</td>
<td>0.001*</td>
<td>34.8±5.4</td>
<td>32.2±6.8</td>
<td>0.037***</td>
</tr>
<tr>
<td><strong>Abdominal fat mass (kg)</strong></td>
<td>4.7±0.6</td>
<td>3.6±1.1</td>
<td>0.015**</td>
<td>4.5±1.0</td>
<td>4.2±1.1</td>
<td>0.115</td>
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<tr>
<td><strong>Lean body mass (kg)</strong></td>
<td>53.3±5.6</td>
<td>52.3±5.8</td>
<td>0.299</td>
<td>55.5±0.9</td>
<td>53.3±0.2</td>
<td>0.019**</td>
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<tr>
<td><strong>Glucose (mmol/L)</strong></td>
<td>4.7±0.3</td>
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<td>0.116</td>
<td>4.6±0.5</td>
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<tr>
<td><strong>Insulin (µU/mL)</strong></td>
<td>8.0±1.8</td>
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<td>0.049**</td>
<td>11.0±4.1</td>
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<tr>
<td><strong>HOMA-IR</strong></td>
<td>1.6±0.3</td>
<td>1.1±0.6</td>
<td>0.034**</td>
<td>2.2±0.8</td>
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<td>0.221</td>
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<tr>
<td><strong>Visfatin (ng/mL)</strong></td>
<td>16.2±3.5</td>
<td>13.7±4.1</td>
<td>0.008*</td>
<td>19.2±2.7</td>
<td>18.1±1.3</td>
<td>0.243</td>
</tr>
</tbody>
</table>

Data are presented as mean ± standard deviation.

*Significant change from pre to post in HIIT and DIO groups (p < 0.01).

**Significant change from pre to post in HIIT and DIO groups (p < 0.05).

***Significant group and time interaction (p < 0.05).

BMI = body mass index; DHIIT = diet and high-intensity interval training combined; DIO = diet-induced only; HOMA-IR = homeostasis model assessment-estimated insulin resistance; (G × T) = group and time interaction.
between abdominal fat loss and decreases in IR after weight-loss program.33

Although the metabolic role of visfatin is not clearly understood, simultaneous reduction of insulin, plasma visfatin levels, and HOMA-IR in the DHIIT group suggests a link between visfatin and insulin sensitivity. A possible explanation for the concurrent changes in plasma visfatin and insulin concentration is provided by Revollo et al.7 They reported a decreased sensitivity of beta cells to glucose by modifying the plasma visfatin level. However, this is in contrast with the findings of Choi et al.13 who reported that 12 weeks of combined exercise training significantly reduced visfatin levels, whereas the IR remained unchanged. Overall, further studies are needed to clarify the role of visfatin in metabolic regulation.

The relatively small number of participants is the main limitation of this study. Although the small size did not damage the clear differences in variables within or between groups due to intervention, our results cannot be generalized to other groups. The major advantages in this study were the directly supervised exercise session and carefully controlled diet of all participants. We recommend further studies using a larger sample. In addition, similar studies conducted on women may provide different results.

In conclusion, this study demonstrates that both DHIIT and DIO reduce weight and body fat in overweight men. However, only DHIIT results in a significant reduction in plasma visfatin, abdominal fat mass, and IR as well as conservation of lean body mass. In addition, DHIIT shows a greater reduction in body weight and total body fat. These observations demonstrate that adding a low-volume 20-minute HIIT (three times/week) to an energy-deficit diet can improve the health benefits of a weight-loss program.

Conflicts of interest

All contributing authors declare no conflicts of interest.

Acknowledgments

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