Effect of Time-Restricted Feeding on Insulin Sensitivity and Oxidative Stress in a Sample of Prediabetes Egyptian Patients

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Abstract

Background: Time-restricted feeding (TRF) is a form of IF, with the daily limiting of food intake (≤10 hours), followed by a daily fast of at least (14 hours). TRF extends the daily fasting period between dinner and breakfast to the following morning; it can be practiced either with or without reducing calorie intake and losing weight.

Aim of Study: The current study aimed to assess the effect of time-restricted feeding on anthropometric measurements, vital data, insulin sensitivity, lipid profile, and oxidative stress in the TRF group compared to the habitual feeding group.

Patients and Methods: A Case-Control Study on 128 selected participants with prediabetes (HBA1c ≥5.7≤6.4%). Were divided into two groups. Group One time-restricted feeding (TRF) and Group Two (habitual feeding) for 12 weeks.

Results: Body weight, waist circumference, HbA1C, PPBG, TG, LDL, and body mass indexreduced in the TRF group in comparison to control group (after 12 weeks) (p-value 0.000**). Systolic Bp, diastolic BP, and pulse (p-value 0.764, 1.000), (p-value 0.769, 0.182) and (p-value 0.768, 0.321) respectively. Also HDL (p-value 0.519, 0.618) and CRP (p-value 0.718, 0.095). Regarding Fasting blood glucose and postprandial insulin after 6 weeks (p-value 0.015*). HOMA-IR and Fasting insulin after 12 weeks (p-value 0.014*, 0.010* respectively). Body weight, BMI and waist circumference (p-value 0.000**), HbA1C (p 0.000**, 0.006**), PPBG and TG (p-value 0.000**) and LDL (p-value 0.000**, 0.002**) respectively. Body weight, BMI and waist circumference (p-value 0.000**), HbA1C (p 0.000**, 0.006**), PPBG and TG (p-value 0.000**) and LDL (p-value 0.000**, 0.002**) respectively. Total cholesterol after 6 weeks (p-value 0.884). Urinary 8 Epi Prostaglandin F2 Alpha (EPA) after 6 weeks (p-value 0.225) and after 12 weeks (p-value 0.006**).

Conclusion: TRF might be beneficial for reducing anthropometric measurements, insulin sensitivity, lipid profile, and oxidative stress in prediabetes patients.

Key Words: Time-restricted feeding – Insulin sensitivity – Oxidative stress – Prediabetes.

Introduction

TIME-restricted feeding (TRF) is a form of IF, with the daily limiting of food intake (≤10 hours), followed by a daily fast of at least (14 hours). TRF extends the daily fasting period between dinner and breakfast to the following morning; it can be practiced either with or without reducing calorie intake and losing weight [1].

TRF reduces body weight, improves glycemic control, lowers insulin levels, prevents hyperlipidemia and improves inflammatory markers in rodents studies using feeding windows of 3-10 hr. report that [2].

Metabolic disorders such as elevated fasting hyperglycemia, hypertriglycetidemimia, hypertension and decreased high density lipoprotein cholesterol are cause of Insulin Resistance (IR). Continued IR can leads to type 2 diabetes (T2D) [3].

Insulin resistance, poor glucose tolerance, β-cell dysfunction have all been linked to oxidative stress [4].

TRF is a well-known method to lose weight and improve insulin sensitivity and oxidative stress. TRF also improves blood pressure, even without weight loss in human studies [5].

Our study aimed to assess the effect of TRF on anthropometric measurements, insulin sensitivity, lipid profile, and oxidative stress in prediabetes patients.

Patients and Methods

A case Control Study that was performed on 128 selected participants with prediabetes (HBA1c ≥5.7≤6.4%). Age (18-65) years, at the Faculty of Medicine Ain Shams University, Egypt from
(April 2020 - February 2022). This protocol was approved by the Research Ethics Committee of the Faculty of Medicine; Ain Shams University (FWA 000017585). All patients wrote informed consent prior to participation in the study.

All Patients were evaluated for their eligibility in the present study. In outpatient clinic of the Internal Medicine and Diabetes Department. Inclusion criteria includes prediabetes.

(HbA1c $\geq 5.7 \leq 6.4\%$), overweight, and obese (BMI $\geq 25$).

The patients who were excluded from the study having the following diseases: Patients with any type of diabetes mellitus (HbA1c $>6.4\%$), Patients with Chronic Heart Failure, Patients with chronic diseases on corticoids (asthma-rheumatoid arthritis-systemic lupus erythematosus... Etc.). Patients with a history of recent infection, Pregnancy or breastfeeding, Severe kidney disease, Severe liver disease, Patients with any diagnosed malignancy, or Treatment with a hypoglycemic agent, insulin sensitizer, or statins. The patients were classified into two groups:

Group One (TRF) consists of 64 prediabetes patients with an 8-hr eating period (12 pm-8 pm same day) and 16 hours of daily fasting from (8 pm the same day 12 pm the next day) for 6 weeks. Then they will return to normal habitual feeding for another 6 weeks. This group will eat 3 small meals during first 6 weeks of study.

- Breakfast (Loaf bread-100gm Bean Meds Or boiled egg-Or 100gm cheese-cup of tea with $\frac{1}{2}$ spoon sugar).
- Lunch (loaf bread or 100gm rice (5 spoons) - green salad - Piece of chicken (100g) or piece of meat (100g) - one fruit).
- Dinner (Loaf bread-100gm cheese or 2 yogurt-salad-cup of tea with $\frac{1}{2}$ spoon sugar).

Group Two (habitual feeding) as a control group: consists of 64 age and sex-matched prediabetes patients with a 12-hr eating window (from 10 am-10 pm same day) and 12 hrs. Of daily fasting for another 6 weeks. This group will eat 3 small meals during eating hours In addition to 2 snacks between meals.

- Breakfast (Loaf bread-100gm Bean Meds Or boiled egg-Or 100gm cheese-cup of tea with $\frac{1}{2}$ spoon sugar).
- Lunch (loaf bread or 100gm rice (5 spoons) - green salad - Piece of chicken (100g) or piece of meat (100g) - one fruit).
- Dinner (loaf bread-100gm cheese or 2 yogurt-salad-cup of tea with $\frac{1}{2}$ spoon sugar).
- Snacks: (Half a Loaf of bread- cheese or egg – salad-fruit).

Aim of 5 meals:

To assess if there are any glycemic benefits in the habitual feeding group without weight loss.

The patients were told to continue their physical activity such as (walking-running) For 30 minutes daily during the study period.

The two study groups were followed up for 12 weeks and each patient had 3 visits:

First visit:

Second visit (1.5 months after 1st visit):

Patients were reviewed about previous anthropometric parameters, lab investigations, and their compliance with time-restricted feeding.

Third visit (1.5 months after 2nd visit):

Patients were reviewed about previous anthropometric parameters and lab investigations.

Blood sampling:

In the morning patients attended the outpatient clinic at hospital following overnight fasting (8-12 hours). Patients were permitted to sit for 10 min, and the patient’s anthropometric parameters and vital data were assessed. Then (~10 ml) venous blood samples were collected.

Anthropometric evaluation:

Anthropometric measurements were evaluated for the selected patient, age (years), weight (kilograms), and height (centimeters), patients were barefoot. While patients were sitting blood pressure measured, following a 15-minute resting period. Body mass index (BMI) was calculated by using the following equation: weight (kg)/square meter of height (m$^2$) $\{6\}$.

Biochemical assays:

Plasma glucose was assessed by the glucose oxidase method. Regarding Serum total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), triglycerides (TG) and LDL-C was calculated by the Friedewald formula $\{6\}$. Plasma insulin (Fasting, postprandial) were analyzed using Enzyme-Linked Immunosorbent Assay (ELISA) kit. Homeostasis model assessment-insulin resistance (HOMA-IR) was computed according to the following formula: fasting glucose (millimoles/
liter) X fasting insulin (microunits/milliliter)/22.5
[7]. The ion exchange method was used to measure HbA1c%, CRP (latex agglutination-ELISA), and urinary 8-Epi Prostaglandin F2 Alpha (EPA) (oxidative stress marker) was analyzed using Enzyme-Linked Immunosorbent Assay (ELISA) kit.

Adverse effects:
The study participants were followed up by telephone and through personal interviews during the study period to assess their adherence to the study and report any participant’s complaints.

Statistical analyses:
The collected data were revised, coded, tabulated, and introduced to a PC using a statistical package for social sciences (IBM SPSS 20.0). Data were presented and suitable analysis was done according to the type of data obtained for each parameter. Continuous data were expressed as means ± SD. Independent sample t-test was used to assess the statistical significance of the difference of a parametric variable between two independent means of two study groups and Paired sample t-test was used to assess the statistical significance of the difference of a parametric variable between two means of one study group before and after the intervention.

The p-value was considered significant as the following: p-value >0.05: Non-significant (NS), p-value <0.05: Significant (S), and p-value <0.001: Highly significant (HS).

Results
At first, 128 patients were included in our study after inclusion and exclusion criteria were set over a three-month.

Baseline data of the participants in both groups:
The Time-restricted feeding group (TRF) revealed no difference in anthropometric baseline data in comparison to habitual feeding group. This study included 128 Participants, 102 female, and 26 male. The mean age was (43.50 ± 8.49 vs 43.73 ± 9.90 years) in the TRF group and habitual feeding group, respectively (p = 0.886), mean body weight was (89.45±15.62 vs 92.00±16.21kg) p-value (0.367). Mean Height was (160.97±5.43 vs 161.58±6.29cm)p-value (0.559) and mean BMI was (35.00±6.01 vs 36.08±6.60kg/m²) P-value (0.336). Mean Waist Circumference was (106.53±11.11 vs 106.67±10.87cm) p-value (0.942) (Table 1).

The Time-restricted feeding group (TRF) showed no significant difference in baseline vital data compared to the habitual feeding group regarding mean diastolic Bp (80.86±5.81 vs 79.98±6.69 mmHg)p-value (0.431) and mean pulse (82.41±4.91 vs 82.73±5.74 bpm) (p-value 0.729), while mean systolic Bp was (120.00±14.80 vs 127.80±15.86 mmHg) with a highly significant difference in habitual feeding group compared to TRF group (p-value 0.005**). (Table 1).

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Table (1): Mean baseline parameters Comparison in two groups.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Time restricted feeding (n = 64)</th>
<th>Habitual feeding (n = 64)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>43.50 ± 8.49</td>
<td>43.73±9.90</td>
<td>0.886</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>89.45±15.62</td>
<td>92.00±16.21</td>
<td>0.367</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>160.97±5.43</td>
<td>161.58±6.29</td>
<td>0.559</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>35.00±6.01</td>
<td>36.08±6.60</td>
<td>0.336</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>106.53±11.11</td>
<td>106.67±10.87</td>
<td>0.942</td>
</tr>
<tr>
<td>Systolic Bp (mmHg)</td>
<td>120.00±14.80</td>
<td>127.80±15.86</td>
<td>0.005**</td>
</tr>
<tr>
<td>Diastolic Bp (mmHg)</td>
<td>80.86±5.81</td>
<td>79.98±6.69</td>
<td>0.431</td>
</tr>
<tr>
<td>Pulse (bpm)</td>
<td>82.41±4.91</td>
<td>82.73±5.74</td>
<td>0.729</td>
</tr>
<tr>
<td>FBG (mg/dl)</td>
<td>95.34±13.23</td>
<td>95.53±11.43</td>
<td>0.932</td>
</tr>
<tr>
<td>PPBG (mg/dl)</td>
<td>116.56±15.40</td>
<td>117.33±29.48</td>
<td>0.854</td>
</tr>
<tr>
<td>F insulin (µIU/ml)</td>
<td>12.87±8.47</td>
<td>13.90±8.98</td>
<td>0.506</td>
</tr>
<tr>
<td>PP insulin (µIU/ml)</td>
<td>43.85±24.16</td>
<td>34.90±26.48</td>
<td>0.048*</td>
</tr>
<tr>
<td>HBA1C (%)</td>
<td>6.04±0.20</td>
<td>6.04±0.23</td>
<td>0.905</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>3.07±2.33</td>
<td>3.19±2.29</td>
<td>0.765</td>
</tr>
<tr>
<td>T cholesterol (mg/dl)</td>
<td>229.8±31.93</td>
<td>212.23±30.52</td>
<td>0.002**</td>
</tr>
<tr>
<td>TG (mg/dl)</td>
<td>167.42±57.38</td>
<td>138.67±52.64</td>
<td>0.004**</td>
</tr>
<tr>
<td>HDL-C (mg/dl)</td>
<td>44.19±5.92</td>
<td>47.55±8.93</td>
<td>0.013*</td>
</tr>
<tr>
<td>LDL-C (mg/dl)</td>
<td>160.53±28.96</td>
<td>139.44±29.68</td>
<td>0.000**</td>
</tr>
<tr>
<td>CRP (mg/dl)</td>
<td>7.37±8.03</td>
<td>8.72±6.63</td>
<td>0.304</td>
</tr>
<tr>
<td>EPA (ng/L)</td>
<td>3506.83±1532.08</td>
<td>3459.30±1608.52</td>
<td>0.864</td>
</tr>
</tbody>
</table>

Chi-square test.
Mean HOMA-IR was (3.07±2.33 vs 3.19±2.29) in TRF group and habitual feeding respectively (p-value 0.765), mean PPBG was (116.56±15.40 vs 117.33±29.48 mg/dl) p-value (0.854), mean of F insulin was (12.87±8.47 vs 13.90±8.98µIU/ml) p-value(0.932), mean HBA1C (6.04±0.22 vs 6.04±0.23%) p-value (0.905). While the Mean of PP insulin was (43.85 ±24.16 vs 34.90±26.48 µIU/ml) which was significantly different (p-value 0.048*). (Table 1).

Regarding Mean T cholesterol (229.8±31.93 vs 212.23±30.52mg/dl) there was a highly significant difference (p-value 0.002**). Mean TG (167.42±57.38 vs 138.67±52.64mg/dl) which was a highly significant difference (p-value 0.004**) mean HDL was (44.19±5.92 vs 47.55±8.93 mg/dl) with a significant difference (p-value 0.013*), mean LDL (160.53±28.96 vs 139.44±29.68mg/dl) which was highly significant difference (p-value 0.000**) and mean CRP (7.37±8.03 vs 8.72±6.63mg/L) with no significant difference between 2 groups (p-value 0.304). (Table 1).

The mean of urinary 8-Epi Prostaglandin F2 Alpha (EPA) was (350.63±1532.08 vs 3459.30±1608.52ng/L), with no statistically significant difference between 2 study groups’ (p-value 0.864) (Table 1).

Body weight, waist circumference and BMI:

The mean (body weight) of both groups were significantly changed after 6 weeks from baseline (7.85±1.58 vs 3.22±1.30kg) (p-value 0.000**) andafter 12 weeks (4.88 ± 2.24 vs 2.14±2.34kg) (p-value 0.000**) (Table 3). Also, the TRF group showed a significant reduction in mean waist circumference by (5.48±1.58) in the TRF group vs (3.16±1.18cm) in the habitual feeding group post-intervention (1) and (2.28±1.23 vs 1.77±2.12cm) post-intervention (2) (p-value 0.000**) but reduction was greater in TRF group in comparison to habitual feeding group (Table 2).

BMI decreased by (3.42±1.48 vs 1.48±1.52kg/m²) post- intervention (1) and (2.28±1.23 vs 1.77 ± 2.12 kg/m²) post- intervention (2) (p-value 0.000**) (Table 3).

Vital data:

After 12 weeks from baseline, the two study groupsp showed no statistically significant change in mean systolic Bp, diastolic BP, and pulse (p-value 0.764, 1.000), (p-value 0.769, 0.182) and (p-value 0.768, 0.321) respectively. (Tables 2,3).

Glycemic control and HOMA-IR:

There was a highly statistically significant change regarding postprandial glucose (PPBG) decreased by (−26, −15%) in TRF group in comparison to habitual feeding group, HbA1c decreased by [−5 vs −3%], HOMA-IR decreased by [−44 vs -10%] and F insulin level decreased by [−37 vs -4%] (p-value 0.000**) after first 6 weeks of study from baseline, changes were higher in TRF group in comparison to habitual feeding group. While a significant change in the mean fasting blood glucose (FBG) decreased by (−7, −5%) and PP insulin decreased by (−30, −21%) (p-value 0.015*). After ending the next 6 weeks of study there was highly significantly differences in mean HbA1c, PPBG, PP insulin, and FBG (p-value 0.006**, 0.000**, 0.000**, and 0.001**) in TRF group more than habitual group, and a significant difference in HOMA-IR and F insulin (p-value 0.014*, 0.010*) in TRF group to habitual feeding group.

We observed increased of F insulin [1%] in the habitual feeding group post-intervention 2 (Tables 2,3).

Lipid profile:

After intervention for first 6 weeks of study, the TRF group show highly significant differences in Total Cholesterol, triglycerides, and LDL-cholesterol (p-value 0.000**) in comparison to habitual feeding group, and no significant difference in HDL-Cholesterol levels between the two groups (p-value 0.519). While after ending the next 6 weeks of study there was highly statistically significant differences between TG and LDL-C (p-value 0.000**, 0.002*) in TRF group to habitual feeding group, and no significant difference in TC and HDL-C levels in both groups (p-value 0.884, 0.618) (Table 2).

Our study reported that the TRF group had a greater reduction in T-cholesterol by [−10, −8 vs −6, −8 %] (p=0.000**, 0.884) compared to the habitual feeding group (Table 3).

The present study results revealed a reduction in triglyceride levels for both groups but a more significant reduction in the TRF group in comparison to the habitual feeding group [−18, −22 vs −4, −5%] (p-value 0.000**).

Our results revealed that the TRF group had a greater decrease in LDL cholesterol compared to the habitual feeding group [−13, −10 vs −6, −6%] (p=0.000**, 0.002*) post intervention (1, 2).

Regarding HDL-cholesterol there were no significant changes between the two groups, HDL levels decreased by (−2, −5%) in the TRF group vs (−3, −4%) in the habitual feeding group (p-value 0.519, 0.618), (Table 3).
### Table (2): Changes in mean variables between two study groups from baseline and post intervention (1, 2).

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mean post intervention (1) from baseline (group 1 vs group 2)</th>
<th>1st (6) weeks p-value</th>
<th>Mean post intervention (2) from baseline (group 1 vs group 2)</th>
<th>2nd (6) weeks p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight(kg)</td>
<td>7.58±1.58 vs 3.22±1.30</td>
<td>-</td>
<td>4.88±2.24 vs 2.14±2.34</td>
<td>0.000**</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>3.42±1.48 vs 1.48±1.52</td>
<td>-</td>
<td>2.28±1.23 vs 1.77±2.12</td>
<td>0.000**</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>5.48±1.58 vs 3.16±1.18</td>
<td>-</td>
<td>2.80±2.76 vs 2.23±1.69</td>
<td>0.000**</td>
</tr>
<tr>
<td>Systolic Bp (mmHg)</td>
<td>2.50±4.80 vs 2.80±6.27</td>
<td>-</td>
<td>-.31±2.50 vs -.31±2.50</td>
<td>1.000</td>
</tr>
<tr>
<td>Diastolic Bp (mmHg)</td>
<td>.78±2.58 vs .61±3.71</td>
<td>-</td>
<td>.00±0.00 vs -.23±1.39</td>
<td>0.182</td>
</tr>
<tr>
<td>Pulse (bpm)</td>
<td>.78±2.58 vs .92±2.80</td>
<td>-</td>
<td>.09±.75 vs .00±0.00</td>
<td>0.321</td>
</tr>
<tr>
<td>FBG (mg/dl)</td>
<td>7.08±6.15 vs 5.11±1.67</td>
<td>0.015*</td>
<td>13.45±10.66 vs 7.31±10.45</td>
<td>0.001**</td>
</tr>
<tr>
<td>PPBG (mg/dl)</td>
<td>29.70±16.59 vs 18.20±9.47</td>
<td>0.000**</td>
<td>13.6±16.57 vs 2.88±11.21</td>
<td>0.000**</td>
</tr>
<tr>
<td>F insulin (µIU/ml)</td>
<td>4.87±6.16 vs .49±3.62</td>
<td>-</td>
<td>1.98±5.84 vs .28±3.81</td>
<td>0.010*</td>
</tr>
<tr>
<td>PP insulin (µIU/ml)</td>
<td>12.43±16.37 vs 6.98±6.42</td>
<td>0.015*</td>
<td>17.62±18.79 vs 5.66±6.09</td>
<td>0.000**</td>
</tr>
<tr>
<td>HBA1C (%)</td>
<td>.35±17.20 vs .20±08</td>
<td>0.000**</td>
<td>.02±33.3±15±3.19</td>
<td>0.006**</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>1.33±1.78 vs .32±94</td>
<td>-</td>
<td>.88±1.72 vs .26±1.05</td>
<td>0.014*</td>
</tr>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>21.52±17.09 vs 12.8±7.32</td>
<td>0.000**</td>
<td>17.34±19.17 vs 16.95±9.58</td>
<td>0.0884</td>
</tr>
<tr>
<td>TG (mg/dl)</td>
<td>30.14±19.65 vs 4.98±4.94</td>
<td>0.000**</td>
<td>37.33±35.68 vs 7.03±9.29</td>
<td>0.000**</td>
</tr>
<tr>
<td>HDL-C (mg/dl)</td>
<td>1.05±5.50 vs 1.50±3.35</td>
<td>0.519</td>
<td>2.39±5.25 vs 2.00±3.26</td>
<td>0.618</td>
</tr>
<tr>
<td>LDL-C (mg/dl)</td>
<td>20.54±16.05 vs 7.71±10.10</td>
<td>0.000**</td>
<td>17.03±19.44 vs 8.21±11.30</td>
<td>0.002*</td>
</tr>
<tr>
<td>CRP (mg/dl)</td>
<td>.6±2.5±5.5 vs .52±88</td>
<td>0.718</td>
<td>.26±2.73 vs .49±1.68</td>
<td>0.995</td>
</tr>
<tr>
<td>EPA (ng/L)</td>
<td>102.48±553.87 vs 954.19±445.67</td>
<td>0.225</td>
<td>525.34±395.98 vs 353.78±286.93</td>
<td>0.006**</td>
</tr>
</tbody>
</table>

Chi-square test.

### Table (3): Differences between mean baseline and post intervention (1, 2) data in both groups.

<table>
<thead>
<tr>
<th>Variables (mean)</th>
<th>Baseline (TRF vs habitual)</th>
<th>1st intervention (1st 6 weeks)</th>
<th>2nd intervention (2nd 6 weeks)</th>
<th>Baseline-1st intervention %</th>
<th>Baseline-2nd intervention %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>89.45 vs 92.00</td>
<td>81.88 vs 88.78</td>
<td>84.57 vs 89.86</td>
<td>-8 vs 4</td>
<td>-5 vs 3</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>35.00 vs 36.08</td>
<td>31.58 vs 34.60</td>
<td>32.72 vs 34.31</td>
<td>-10 vs 3</td>
<td>-8 vs 3</td>
</tr>
<tr>
<td>Waist Circumference (cm)</td>
<td>106.53 vs 106.67</td>
<td>101.05 vs 103.52</td>
<td>103.73 vs 104.44</td>
<td>-5 vs 3</td>
<td>-3 vs 2</td>
</tr>
<tr>
<td>Systolic Bp (mmHg)</td>
<td>120.00 vs 127.80</td>
<td>117.50 vs 125.00</td>
<td>120.31 vs 128.11</td>
<td>-2 vs 2</td>
<td>0</td>
</tr>
<tr>
<td>Diastolic Bp (mmHg)</td>
<td>80.86 vs 79.98</td>
<td>80.08 vs 79.37</td>
<td>80.86 vs 80.22</td>
<td>-0.9 vs 0</td>
<td>0</td>
</tr>
<tr>
<td>Pulse (bpm)</td>
<td>82.41 vs 82.73</td>
<td>81.62 vs 81.81</td>
<td>82.50 vs 82.73</td>
<td>-1 vs 1</td>
<td>0</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>3.07 vs 3.19</td>
<td>1.74 vs 2.88</td>
<td>2.19 vs 2.93</td>
<td>-4 vs 10</td>
<td>-30 vs 10</td>
</tr>
<tr>
<td>EPA (ng/L)</td>
<td>3506.83 vs 3459.30</td>
<td>2444.34 vs 2505.11</td>
<td>2981.48 vs 3105.52</td>
<td>-30 vs 27</td>
<td>-15 vs 10</td>
</tr>
<tr>
<td>HbA1C (%)</td>
<td>6.04 vs 6.04</td>
<td>5.69 vs 5.84</td>
<td>6.01 vs 5.89</td>
<td>-5 vs 3</td>
<td>0</td>
</tr>
<tr>
<td>FBG (mg/dl)</td>
<td>95.34 vs 95.53</td>
<td>88.27 vs 90.42</td>
<td>81.89 vs 88.22</td>
<td>-7 vs 5</td>
<td>1</td>
</tr>
<tr>
<td>PPBG (mg/dl)</td>
<td>116.56 vs 117.33</td>
<td>86.86 vs 99.12</td>
<td>102.95 vs 114.45</td>
<td>-26 vs 15</td>
<td>1</td>
</tr>
<tr>
<td>F insulin (Uiu/ml)</td>
<td>12.87 vs 13.90</td>
<td>8.00 vs 13.41</td>
<td>10.89 vs 14.19</td>
<td>-37 vs 4</td>
<td>1</td>
</tr>
<tr>
<td>Pp insulin (Uiu/ml)</td>
<td>43.85 vs 34.90</td>
<td>31.42 vs 27.92</td>
<td>26.23 vs 29.24</td>
<td>-30 vs 21</td>
<td>5</td>
</tr>
<tr>
<td>TG (mg/dl)</td>
<td>167.42 vs 138.67</td>
<td>137.28 vs 133.69</td>
<td>130.09 vs 131.64</td>
<td>-18 vs 4</td>
<td>1</td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td>44.19 vs 47.55</td>
<td>43.14 vs 46.05</td>
<td>41.80 vs 45.55</td>
<td>-2 vs 3</td>
<td>1</td>
</tr>
<tr>
<td>LDL (mg/dl)</td>
<td>160.53 vs 139.44</td>
<td>139.98 vs 131.73</td>
<td>143.50 vs 131.23</td>
<td>-13 vs 6</td>
<td>1</td>
</tr>
<tr>
<td>CRP (mg/dl)</td>
<td>7.37±8.72</td>
<td>6.73±8.20</td>
<td>7.11±7.78</td>
<td>-11 vs 5</td>
<td>0 vs 10</td>
</tr>
</tbody>
</table>
Inflammatory and oxidative stress markers:

Regarding CRP levels there was no significant difference between the two study groups after 12 weeks of study (p-value 0.718, 0.095) the decrease in CRP levels was higher in TRF group comparing to habitual feeding group after first 6 weeks of study \([-11, 0 \text{ vs } -5, 10\%]\) while CRP levels reduced more in habitual feeding group to TRF group after ending the study.

Regarding EPA there was no significant difference between 2 study groups after first six weeks of study (p-value 0.225). While a highly significant difference after ending the study (p-value 0.006**) Reduction in EPA levels was higher in TRF group to habitual feeding group post intervention (1,2) (Table 2.3).

The present study showed that levels of 8 Epi Prostaglandin F2 Alpha (EPA) reductions was higher in the TRF group compared to the habitual feeding group. EPA levels decreased by \([-30, -15 \text{ vs } -27, -10\%]\) (p-value 0.225, 0.006**) from baseline (Table 3).

Discussion

In our study, the effect of TRF on anthropometric measurements, vital data, indicators of glycemic control, insulin resistance, Inflammatory, oxidative stress markers, and lipid profile in prediabetes patients were analyzed.

The study results showed that the TRF group in prediabetes patients significantly improved anthropometric measurements, insulin sensitivity, lipid profile, and oxidative stress.

Our results showed a reduction in mean body weight in the TRF group compared to the habitual feeding group post-intervention [1] Which is consistent with the results of some other research [8,9,10].

On the contrary, Lowe et al., reported no weight loss, with no significantly difference in control group [11].

Also, the TRF group showed a significant reduction in mean waist circumference in the TRF group vs the habitual feeding group post-intervention [1] and post-intervention [2].

Our results in consistency with (Kesztyus et al.) They found a decrease in mean waist circumference in 40 Participants \((-5.3\pm3.1cm)\) (p<0.001) [12].

And Cienfuegos S. et al., found that four-six-hour TRF in 58 participants were highly statistically significant on BMI in TRF and control groups [13].

Our results showed non-significant reductions in mean systolic BP, diastolic BP and pulse in TRF group to habitual feeding group after 12 weeks from intervention.

Michael J. Wilkinson. Showed that TRF has a significant decrease in systolic and diastolic blood pressure \([-4\%\text{–}8\%]\) respectively [14] which is inconsistency with our results.

Our study results revealed a highly HOMA-IR significant reduction in the TRF group in comparison to habitual feeding study group \([-44, 10\%]\) post intervention 1 and \([-30, 10]\%\) post intervention 2. Jamshed et al., [15] supported our results, which found a significant HOMA-IR reduction (p<0.001).

The study results showed a statistically significant decrease in Fasting blood glucose in both groups but more significant in the TRF group. PPBG and HbA1c decreased In the TRF group compared to the habitual feeding group. Which are in consistent with Antoni RRT et al. [16] who found decreased fasting plasma glucose concentration. Compared with controls who maintained habitual feeding patterns.

HbA1c reduced in the time-restricted feeding group compared to the control group over 12 weeks (p< 0.001) according to Che, T. et al. [17] which was consistent with our study.

Our results inconsistency with Carlson et al. [18] that found TRE with late eating was shown to increase fasting glucose. And TRF has no effect or worsened PP glucose levels.

The present study showed improvement in insulin levels in both groups but more in the TRF group than the habitual feeding group. F insulin decreased by \((-37, -22\%)\) in the TRF group vs \((-4\%)\) in the habitual feeding group while PP insulin decreased by \([-30, -40 \text{ vs } -21, -16\%]\) in the TRF group in comparison to habitual feeding group.

We observed increased of F insulin \([1\%]\) in the habitual feeding group post-intervention 2.

Our results in consistent with Sutton et al., that found 5-weeks, randomized TRF in prediabetes men, isocaloric and eucaloric controlled feeding reduced fasting insulin by (3.4±1.6mU/l) (p=0.05) and PP insulin levels (p≤0.01) [19].

Importantly, our results showed important improvement in lipid profile (TG, T-cholesterol, and LDL-cholesterol) which are cardiovascular disease risk markers.

Our study reported that the TRF group had a greater reduction in T-cholesterol.

A previous study by Wilkinson et al., [20] showed that 10 hrs. TRF decreased plasma cholesterol which was consistent with our study.
Gabel K et al. [21] found that eight hours TRF did not affect plasma cholesterol levels between the 2 groups.

The present study results revealed a reduction in triglyceride levels for both groups but a more significant reduction in the TRF group in comparison to the habitual feeding group [−18, −22 vs −4, −5%].

Our results revealed that the TRF group had a greater decrease in LDL cholesterol compared to the habitual feeding group [−13, −10 vs −6, −6%].

Our results are in agreement with (Wilkinson et al., 2019), which found that Ten-hour TRF in 35 participants caused significant reductions in low-density lipoprotein cholesterol (LDL-C) (−11.94±19.01mg/dL (−11%), \(p=0.016\)).

Our results were incompatible with (Gabel K et al.). Which found that eight hours of time-restricted feeding did not affect plasma LDL cholesterol compared to a matched historical control group.

Regarding HDL-cholesterol there were no significant changes between the two groups, HDL levels decreased by (−2, −5%) in the TRF group vs (−3, −4%) in the habitual feeding group.

Our results showed that TRF in group (1) and habitual feeding in group (2) had no significant effect on CRP levels, but reduction in CRP levels was higher in TRF group.

Our results were supported by (Sutton et al., 2018 and Wilkinson et al., 2020) who found that CRP concentrations did not change after 5–12 weeks of TRE.

Oxidative stress is defined as the increased generation of free radicals and impaired antioxidant defense it plays a leading role in the progression of DM and its complication [23].

Regarding oxidative stress, 8 Epi Prostaglandin F2 Alpha (EPA) is widely used as an oxidative stress biomarker [24].

8-iso-prostaglandin-F2α (8-iso-PGF2α), as one of the stable products of non-cyclooxygenase peroxidation of arachidonic acid, has proved to be the most available and reliable marker of lipid peroxidation in vivo and it appears more sensitive and specific than other markers of oxidative stress [25].

The present study showed that levels of 8 Epi Prostaglandin F2 Alpha (EPA) reduction was higher in the TRF group compared to the habitual feeding group. EPA levels decreased by [−30, −15 vs −27, −10%].

Our results were supported by (Cienfuegos et al., 2020) who measured oxidative stress markers and found significant decreases in oxidative markers after 5-8 weeks of TRF.

Several limitations of our research should be noted. Being a case-control study therefore causality could not be certainly determined. It is necessary to carry out a study with prospective nature in the future. Also, the time of intervention was short, and further follow-up is needed to observe the long-term results of TRF.

Conclusion:

TRF is helpful in reduction anthropometric measurements, improving glycemic control and insulin resistance in prediabetes. Also, TRF provides primary prevention of cardiovascular events in prediabetes by improving lipid profiles and improve oxidative stress markers.

Availability of data:

The data of this study finding are available upon request.

References

8- CHOW L.S., MANOOGIAN E.N., ALVEAR A., FLEISCHER J.G., THOR H., DIETSCHKE K., WANG Q., HODGE-ES I.S., ESCH N. and MALAEB S.: Time-restricted eating effects on body composition and metabolic measures in...
تأثير التغذية المقيدة زمنياً على حساسية الأنسولين والتأكد في عينيه من المرضى المصريين الذين يعانون من خطوراً اصابته بداء السكري

الهدف من الدراسة: تهدف الدراسة الحالية إلى تقديم تأثير التغذية المقيدة زمنياً على قياسات الجسم البشري، البيانات الجبليبية، حساسية الأنسولين، ملف الدهون والإجهاد التأكسدي في مجموعة تطبيق التغذية المقيدة زمنياً مقارنة بمجموعة تطبيق التغذية المعتادة.

الرياضيات والطرق: تم إجراء دراسة الحالات والشواهد على 128 مشاركًا مختارًا يعانون من خطرة اصابته بداء السكري. تتأثر نسبة السكر التراكي فيهم بين (6.5-7.6 %). تم تقسيمهم إلى مجموعتين، المجموعة الأولى تطبق التغذية المقيدة زمنياً لمدة 6 أسابيع والمجموعه الثانية تطبق نظام التغذية المعتادة لمدة 12 أسبوع.

النتائج: انخفض وزن الجسم، محيط الخصر، ونسبة السكر التراكي، الدسم، السكر الفاطر، الدهون الثلاثية، الكوليسترول، منخفض الكافيه، ومؤشر كتلة الجسم في مجموعة التغذية المقيدة زمنياً مقارنة بالمجموعة الضابطة (بعد 12 أسابيع) من بداية الدراسة.

بعد 12 أسبوع من تطبيق الدراسة للمجموعتين لم يكن هناك اختلاف هام في النتائج بين المجموعتين فيما يتعلق بضغط الدم الانقباضي، ضغط الدم الانبساطي، والتبخش. أيضاً، نتائج الوراثة الديني على الكافيه ووراثة السمنة التفاعلية لم يكن هناك اختلاف هام بين المجموعتين. بينما ظهر اختلاف هام في النتائج بين المجموعتين في مستوى السكر الدم ونسبة الدهون الفاطر.

بعد 12 أسبوع من بداية الدراسة كان هناك اختلاف هام بين المجموعتين، ونسبة الدهون الفاطر بالجملة بعد 12 أسبوع من الدراسة كان هناك اختلاف واضح فيما يتعلق بوزن الجسم، مؤشر كتلة الجسم، محيط الخصر، السكر التراكي، السكر الفاطر والكوليسترول الناتجي منخفض الكافيه.

فيما يتعلق بالكوليسترول الكلي، كان هناك اختلاف هام في النتائج بين المجموعتين بعد 6 أسابيع من الدراسة حيث انخفض في المجموعة الأولى مقارنة بالمجموعة الثانية ولكن لم يكن هناك اختلاف في النتائج بعد انتهاء الدراسة بين المجموعتين.

وبقياس نسبة الزيروستات النفا في البول (مؤشر جيوي للاجهاد التأكسدي) بعد 6 أسابيع من الدراسة لم يكن هناك اختلاف هام في النتائج بين المجموعتين. ولكن ظهر اختلاف هام في نتائج الزيروستات النفا في البول بعد 12 أسبوع في المجموعة الأولى مقارنة بالمجموعة الثانية.

الاستنتاج: تعتبر التغذية المقيدة زمنياً مفيدة في تقليل قياسات الجسم (الوزن - مؤشر كتلة الجسم - محيط الخصر)، تحسن حساسية الأنسولين، تحسن مستوى الكوليسترول والدهون بالدم، وفعالية في تحسن الإجهاد التأكسدي في المرضى الذين يعانون من خطرة الاصابة بداء السكري.