# Greater Weight Loss and Hormonal Changes After 6 Months Diet With Carbohydrates Eaten Mostly at Dinner

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**This study was designed to investigate the effect of a low-calorie diet with carbohydrates eaten mostly at dinner on anthropometric, hunger/satiety, biochemical, and inflammatory parameters. Hormonal secretions were also evaluated. Seventy-eight police officers (BMI >30) were randomly assigned to experimental (carbohydrates eaten mostly at dinner) or control weight loss diets for 6 months. On day 0, 7, 90, and 180 blood samples and hunger scores were collected every 4 h from 0800 to 2000 hours. Anthropometric measurements were collected throughout the study. Greater weight loss, abdominal circumference, and body fat mass reductions were observed in the experimental diet in comparison to controls. Hunger scores were lower and greater improvements in fasting glucose, average daily insulin concentrations, and homeostasis model assessment for insulin resistance ($HOMA_{IR}$), T-cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, C-reactive protein (CRP), tumor necrosis factor-α (TNF-α), and interleukin-6 (IL-6) levels were observed in comparison to controls. The experimental diet modified daily leptin and adiponectin concentrations compared to those observed at baseline and to a control diet. A simple dietary manipulation of carbohydrate distribution appears to have additional benefits when compared to a conventional weight loss diet in individuals suffering from obesity. It might also be beneficial for individuals suffering from insulin resistance and the metabolic syndrome. Further research is required to confirm and clarify the mechanisms by which this relatively simple diet approach enhances satiety, leads to better anthropometric outcomes, and achieves improved metabolic response, compared to a more conventional dietary approach.**

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## INTRODUCTION

Manipulation of physiological pathways in order to reduce obesity and symptoms of the metabolic syndrome is a major focus of research worldwide. Recent data show that adipose tissue, the energy storage site of the body, is also an endocrine organ that synthesizes and secretes a variety of adipocytokines. This includes hormones that regulate hunger and satiety as well as those associated with the development of insulin resistance, the metabolic syndrome and inflammation (1).

Leptin "the satiety hormone" has been described as the "information provider" of adipose tissue status to receptors in the brain. In short term, it regulates hunger, satiety, and food intake (1–3). Previous studies have described a typical diurnal pattern of leptin secretion that falls during the day from 0800 to 1600 hours, reaching a nadir at 1300 hours and increases from 1600 with a zenith at 0100 hours (4,5). Ironically, this crucial hormone responsible for satiety is at its highest levels when individuals are sleeping.

Adiponectin is considered to be "the link between obesity, insulin resistance, and the metabolic syndrome" (6). Adiponectin plays a role in energy regulation as well as in lipid and carbohydrate metabolism, reducing serum glucose and lipids, improving insulin sensitivity and having an anti-inflammatory effect (7). Adiponectin's diurnal secretion pattern has been described in obese individuals (particularly with abdominal obesity), as low throughout the day. In normal weight subjects or overweight subjects following weight loss, a general increase in adiponectin concentrations is detected as well as a rise in the diurnal pattern during the daytime, with zeniths at 1100 and 0100 hours and a decline at night, reaching a nadir at 0400 hours (5,8).

Innovative dietary regimens that will be able to modify these hormonal secretion patterns may be beneficial to people

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suffering from severe/morbid obesity. The idea of studying the effect of a low-calorie diet with carbohydrates eaten mostly at dinner on hormonal diurnal secretion patterns came about after analyzing results from studies with Muslim populations during Ramadan (fasting during the day and consuming an enriched carbohydrate dinner). These studies have demonstrated that the diurnal pattern of leptin secretion can be changed (9,10). In addition, euglycemic hyperinsulinemic clamp studies have demonstrated elevated serum leptin concentrations after 6–8 h (4). No information exists neither regarding modification of the diurnal secretion patterns of adiponectin, nor of changes in hunger/satiety anthropometric, biochemical or inflammatory parameters under comparable conditions.

This study was designed to estimate the effects of a weight loss diet with carbohydrates eaten mostly at dinner (the experimental diet) on anthropometric measurements, hunger scores and parameters related to insulin resistance, the metabolic syndrome and inflammation. Leptin and adiponectin secretions were also investigated.

It was hypothesized that consumption of carbohydrates mostly in the evening would modify the typical diurnal pattern of leptin secretion as observed in Muslim populations during Ramadan. The experimental diet induced a single daily insulin secretion in the evening, thus it was predicted that the diet would lead to higher relative concentrations of leptin starting 6–8 h later i.e., in the morning and throughout the day. This may lead to enhanced satiety during daylight hours and improve dietary adherence.

Studies have shown that there is a negative correlation between insulin and adiponectin levels (11). Since the experimental diet used in this study reduces insulin secretion during the day, it was also hypothesized that adiponectin concentrations would increase throughout the day improving insulin resistance, diminishing symptoms of the metabolic syndrome and lowering inflammatory markers.

## METHODS AND PROCEDURES

One hundred police officers (men and women), aged 25–55, BMI >30 from the Israeli Police Force, Tel-Aviv District, enrolled in the study in May 2006. All participants signed informed consent forms (approved by the Regional Committee for Human Experimentation, Kaplan Hospital (Rehovot, Israel), in accordance with the Helsinki declaration). Individuals with cardiovascular diseases, hypertension, diabetes

**Table 1 Experimental/control diets**

| | |
|---|---|
| **Experimental diet** | |
| Breakfast | Coffee/tea + artificial sweetener + 1/5 cup of low fat milk + 7 walnut halves/7 almonds |
| Morning snack (1000 hours) | Plain low fat yogurt/white cheese (1/2 cup) + vegetable |
| Lunch | Meat/fish dish (without coating, excluding ground meat) + boiled vegetables/vegetable soup + vegetable salad + 1 teaspoon of oil/tablespoon of dressing (from the permitted list) |
| Afternoon snack (1600 hours) | Coffee/tea + artificial sweetener + 1/5 cup of low fat milk + 7 walnut halves/7 almonds |
| Dinner | Coffee/tea + artificial sweetener + 1/5 cup of low fat milk + alternative A or B |
| | Alternative A: |
| | 2–4 pieces of bread/4–8 pieces of reduced calorie bread + 1/2 cup of white cheese/1 slice of yellow cheese/ 2 tablespoons of humus/egg/1/2 a can of tuna fish/4 slices of pastrami + vegetable salad + 1 teaspoon of oil/ tablespoon of tehina/1/4 avocado/1 tablespoon of dressing + fruit/fruit yogurt/diet ice-cream/2 biscuits/1 cookie |
| | Alternative B: |
| | 1–2 cups of cooked rice/pasta/puree/corn/legumes/1–2 potato/1–2 sweet potato + 1 tablespoon of gravy + boiled vegetables/vegetables salad + 1 teaspoon of oil/ tablespoon of tehina/1/4 avocado/1 tablespoon of dressing + fruit yogurt/diet ice-cream/2 biscuits/1 cookie |
| Night snack (upon need) | Coffee/tea + artificial sweetener + 1/5 cup of low fat milk + 7 walnut halves/7 almonds + plain yogurt/white cheese (1/2 cup) |
| Beverages | Water/no-calorie diet drinks |
| **Control diet** | |
| Breakfast | Coffee/tea + artificial sweetener + low fat milk +1 piece of bread/2 pieces of reduced calorie bread/2 crackers/ 2 biscuits + white cheese |
| Morning snack (1000 hours) | Plain yogurt/fruit yogurt + 7 walnut halves/7 almonds |
| Lunch | Meat/fish dish + boiled vegetables/vegetable soup + vegetable salad + 1 teaspoon of oil/tablespoon of dressing + 1/2 cup of cooked rice/pasta/ puree/corn/legumes/1/2 potato/1/2 sweet potato |
| Afternoon snack (1600 hours) | Coffee/tea + artificial sweetener + low fat milk + 2 biscuits/fruit + 7 walnut halves/7 almonds |
| Dinner | Coffee/tea + artificial sweetener + low fat milk + 1-2 piece of bread/2–4 pieces of light bread/2–4 crackers + 1/2 cup of white cheese /1 slice of yellow cheese/2 tablespoons of humus/egg/1/2 a can of tuna fish/4 slices of sliced turkey breast + vegetable salad + 1 teaspoon of oil/tablespoon of tehina/1/4 avocado/tablespoon of dressing |
| Night snack (If needed) | Coffee/tea + artificial sweetener + low fat milk + 7 walnut halves/7 almonds + plain yogurt/fruit yogurt/diet ice-cream |
| Beverages | Water/no-calorie diet drinks |

mellitus or other primary diseases, pregnant women, and individuals who followed any type of diet regimen within a year prior to the study were excluded from the study. Seventy-eight individuals met study criteria and took part in the 6-month randomized clinical trial. On day 0, the police officers participated in a day-long event at an Israeli police vacation resort. Participants met the project dietitian, completed questionnaires, underwent anthropometric measurements and were then randomly assigned to the experimental group or the control group. The experimental group was prescribed a standard low-calorie diet (20% protein, 30–35% fat, 45–50% carbohydrates, 1,300–1,500 kcal) providing carbohydrates mostly at dinner, whereas the control group received a standard low-calorie diet (20% protein, 30–35% fat, 45–50% carbohydrates, 1,300–1,500 kcal), providing carbohydrates throughout the day (Table 1). Blood samples were collected and the participants filled out hunger-satiety scales (H-SS) every 4 h before meals. The day was filled with a variety of lectures, workshops, and entertainment activities. Blood samples and H-SS (as on day 0) were taken again on day 7, 90, and 180. The dietitian met all participants personally at 1–3-week intervals and at each of the study time points (the 4 day-long events) in order to perform a comprehensive inquiry and estimate adherence to dietary regimen and caloric intake. Participants, who did not attend meetings with the dietitian, did not adhere to the diet or exceeded the caloric range of 1,300–1,500 kcal/day, were excluded from the study. Anthropometric measurements were recorded regularly.

### Blood sampling and biochemical analysis

Fasting (12 h) blood samples were taken at 0800 hours and in intervals of 4 h (at 1200, 1600 and 2000 hours), before meals, on each of the full-day events. Blood was centrifuged (400*g*) and serum was collected and stored at −20 °C for further analysis of leptin and adiponectin (high molecular weight) concentrations, using Linco research sandwich ELISA kits (Millipore-Linco, Billerica, MA). Insulin, glucose, total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, triglycerides, and C-reactive protein (CRP) were tested in Meuhedet Medical Services laboratories (Rehovot, Israel) using the standard procedures of the laboratory. Insulin was analyzed using Abbot Microparticle Enzyme Immunoassay test kits (Ilex, Rosh Ha'ayin, Israel). Glucose was analyzed by Olympus enzymatic UV test kits, cholesterol, HDL-cholesterol, LDL-cholesterol and triglycerides were analyzed by Olympus enzymatic color test kits, and CRP was analyzed using Olympus Immunoturbidimetric test kits (Medtechnica, Petah Tiqwa, Israel). Insulin resistance was evaluated using the homeostasis model assessment for insulin resistance ($HOMA_{IR}$) (calculated from morning glucose and insulin values). $HOMA_{IR}$ calculator ver. 2.2 was downloaded from the Diabetes Trials Unit-The Oxford Center for Diabetes, Endocrinology, and Metabolism website (12). Tumor necrosis factor-α (TNF-α) high sensitive and interleukin-6 (IL-6) high sensitive were measured using R&D systems sandwich ELISA kits (Minneapolis, MN).

### H-SS

Hunger-Satiety questionnaires, adapted from Paul E. Garfinkel (13) and translated into Hebrew, were filed at 0800 hours and in intervals of 4 h (at 1200, 1600, and 2000 hours), before meals. The participants chose statements that best described how they felt at each time point. Hunger-Satiety Score (H-SSc) is a scale of descriptions that ranges from starving (1 point) to devastatingly full (10 points). High H-SSc indicates less hunger and greater satiety. Other questions analyzed dealt with "urge to eat" and "preoccupation with thoughts about food."

### Statistical analysis

Of the 78 subjects who met study criteria, 63 completed the program (Figure 1). This sample size was sufficient to detect a difference of 3 kg between mean weight reductions in the two groups with 75% power, assuming a standard deviation of 4.5 kg. Anthropometric parameters were expressed as an absolute reduction and as percent reduction. For analysis of biochemical changes, 12-h hormonal average, inflammatory and H-SSc parameters, values on day 90 and day 180 were expressed as percentage of baseline. For cholesterol parameters, as changes due to diet were expected to be long term, the average of day 0 and day 7 values were used as a more reliable baseline. Changes in scores for "urge to eat" and "preoccupation with food" (1 = none, 2 = mild, 3 = moderate, 4 = very strong) were analyzed ordinally and categorically (stronger/not stronger). All categorical variables were compared between groups by the $\chi^2$ test. Additional differences between the groups at baseline were analyzed by a *t*-test. For parameters where significant differences were discovered, the baseline value was used as a covariate in the ensuing analyses. Differences in anthropometric parameters were analyzed by two-way ANOVA (treatment, gender). For biochemical and inflammatory parameters, 12-h hormonal average and H-SSc, repeated measures ANOVA over days (and also over hours, for H-SSc) was used to compare treatments, with sex as an additional factor. Differences between groups on specific days (and specific hours, for H-SSc) were performed by preplanned contrast *t*-tests. Significance of difference from baseline was established using a *t*-test with standard error derived from the ANOVA model. Differences in ordinal scale variables were analyzed by the Wilcoxon Rank Sum test. Statistical significance was set at $P < 0.05$. In the description of the study population, we used standard deviation as a measure of dispersion. In reporting the results, we used the standard error to enable assessment of the difference between the group means. For all data analyses statistical programs SAS 9.1 and JMP 7.0.1 (SAS Institute, Cary, NC) were used.

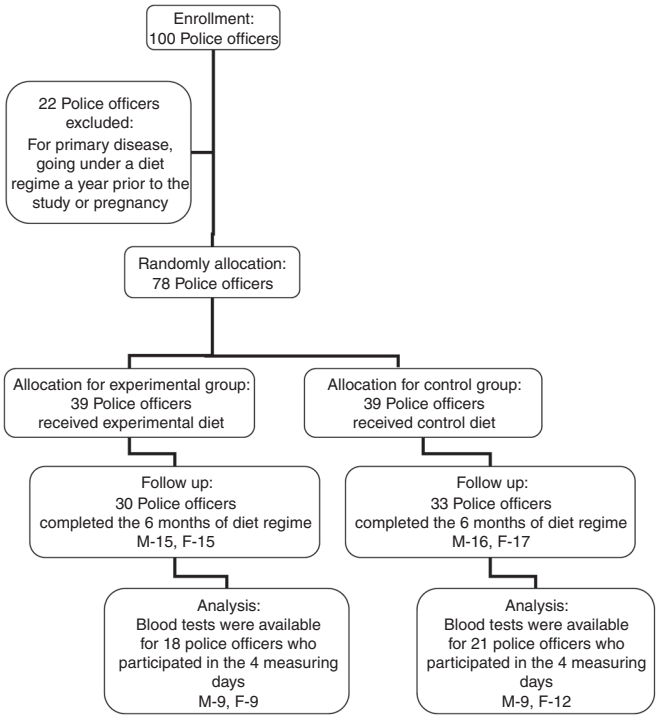


**Figure 1** A flow diagram of the study.

## RESULTS

A flow diagram of the study is shown in Figure 1. Out of 100 enrolled police officers, 78 met inclusion criteria and were randomly allocated to the experimental or control diet groups. Of those who completed the 6-month diet regimen, anthropometric measurements were available for 30 subjects in the experimental group and 33 subjects in the control group. The difference in dropout rates was nonsignificant between groups ($P = 0.39$). Complete blood data were available for 39 subjects who participated in the four full-day events. Baseline

**Table 2 Baseline demographic, anthropometric, hormonal, biochemical, inflammatory, and H-SSc characteristics of participants**

| | Experimental group ($n$ = 30) | Control group ($n$ = 33) |
|---|---|---|
| Age (years) | 43.0 ± 7.50 | 42.5 ± 6.61 |
| Men, $n$ (%) | 15 (50.0%) | 17 (51.5%) |
| Weight (kg) | 98.3 ± 18.0 | 91.0 ± 14.0 |
| BMI (g/m$^2$) | 34.2 ± 4.30 | 32.1 ± 3.17* |
| Abdominal circumference (cm) | 111.1 ± 12.8 | 105.5 ± 8.60* |
| Body fat percent (%) | 39.6 ± 6.02 | 37.3 ± 5.82 |
| | **Experimental group ($n$ = 18)** | **Control group ($n$ = 21)** |
| Insulin (μU/ml) | 29.8 ± 23.4 | 23.2 ± 20.0 |
| Leptin (ng/ml) | 26.9 ± 18.7 | 29.3 ± 12.1 |
| Adiponectin (ng/ml) | 46.7 ± 24.6 | 47.2 ± 33.5 |
| Glucose (mmol/l) | 5.06 ± 1.05 | 4.85 ± 1.09 |
| $HOMA_{IR}$ | 1.68 ± 0.94 | 1.33 ± 0.86 |
| Triglycerides (mmol/l) | 1.88 ± 0.68 | 2.00 ± 0.74 |
| Total cholesterol (mmol/l) | 5.34 ± 0.77 | 5.05 ± 0.62 |
| LDL-cholesterol (mmol/l) | 3.67 ± 0.76 | 3.30 ± 0.57 |
| HDL-cholesterol (mmol/l) | 0.77 ± 0.23 | 0.85 ± 0.21 |
| CRP[a] (mg/l) | 8.20 ± 8.42 | 3.44 ± 2.90* |
| TNF-α (pg/ml) | 1.89 ± 0.63 | 1.93 ± 1.11 |
| IL-6 (pg/ml) | 2.71 ± 1.39 | 2.53 ± 1.17 |
| H-SSc | 5.29 ± 0.73 | 5.34 ± 0.75 |

Mean ± s.d. or number (percent). To convert values for glucose, triglycerides, total cholesterol, LDL-cholesterol, and HDL-cholesterol to mg/dl, divide by 0.05551, 0.01129, 0.02586, 0.02564, and 0.02564, respectively.
CRP, C-reactive protein; HDL, high-density lipoprotein; $HOMA_{IR}$, homeostasis model assessment for insulin resistance; H-SSc, hunger-satiety score; IL-6, interleukin 6; LDL, low-density lipoprotein; TNF-α, tumor necrosis factor-α.
[a]Log transformation was used before analysis to normalize and to stabilize variances.
*Significant difference between groups at baseline ($P < 0.05$).

demographic, anthropometric, hormonal, biochemical, inflammatory, and hunger/satiety characteristics of the trial groups are presented in Table 2. No significant differences were observed at baseline between the groups except for BMI, abdominal circumference, and CRP. Adjustment for these differences was made using analysis of covariance in order to prevent bias in estimating the treatment effect.

### Anthropometric parameters

Anthropometric changes after 6 months are presented in Table 3. Significant weight loss, BMI, abdominal circumference, and body fat percentage reductions were found in both groups. Significantly greater weight loss was observed in the experimental group vs. the control group at the end of the study (11.6 vs. 9.06 kg, $P = 0.024$). Trends of greater absolute BMI reduction (3.99 vs. 3.16) and abdominal circumference reduction (11.7 vs. 9.39 cm) were observed in the experimental group. These trends were not significant after adjusting for differences in baseline values. A trend toward greater reduction in absolute body fat percent (6.98 vs. 5.13%) was observed at the end of the study in the experimental diet group.

### H-SS

Higher H-SSc generally indicate that subjects were less hungry and more satiated. After 180 days on the experimental diet, the H-SSc was 13.7% higher compared to the first week on diet ($P < 0.05$) (Figure 2a). The control group, however, reported a 5.9% lower H-SSc compared to baseline. It was found that control group participants felt significantly more hungry at noon on day 90 and 180 compared to the first week (19.3% and 22.4% less in H-SSc respectively, $P < 0.05$) (Figure 2b). It was also found that in the afternoon the experimental group felt less hungry on days 90 and 180 compared to the first week (27.7 and 25.1% more in H-SSc respectively, $P < 0.05$). The experimental group felt less hungry in the evening of day 180 compared to the first week as well (28.0% higher H-SSc, $P < 0.05$). A significant difference between the groups in the H-SSc change from baseline was found on day 180 in the evening (28.0% increase vs. 6.6% decrease in H-SSc respectively, $P = 0.03$). Analysis of the question, evaluating "the urge to eat," revealed significant differences between the groups on day 180 in the afternoon. In the experimental diet group, 67% of the participants had a reduced urge to eat (median difference 0.5 on a 1–4 scale), compared to the first week (average day 0 and 7 at the same hour), whereas only 19% of the control group participants had a lower urge to eat (median difference 0) compared to the first week ($P < 0.05$ by the $\chi^2$ test and by the Wilcoxon Rank Sum test). When the question of "preoccupation with thoughts about food" was analyzed, differences between groups were observed on day 180 in the afternoon. In the experimental group, none of the participants had enhanced preoccupation with thoughts about food (median difference 0.5 on a 1–4 scale), compared to the first week (average day 0 and 7 at the same hours), whereas 33% of the control group participants had a higher preoccupation with food (median difference 0) compared to the first week (borderline significant by the Wilcoxon Rank-Sum test ($P = 0.067$) and $\chi^2$ test ($P = 0.052$)).

### Serum biochemical parameters level

Biochemical measurements are presented in Table 4. Day 180 on the experimental diet, revealed significantly lower average daily insulin concentrations when compared to baseline (68.0%, $P < 0.05$). Insulin concentrations were also significantly lower in comparison to the control group on day 180 (68.0% from baseline vs. 122.6% from baseline, $P = 0.006$). The experimental diet led to a significant decrease (20%, $P < 0.01$) in fasting glucose concentrations after 180 days compared to baseline. In comparison, the control diet led to 8.3% decrease, which did not reach significance. A similar trend was observed on day 90 (11.4 vs. 3.3% decrease respectively). After 90 days on the diet, a 30.9% decrease in $HOMA_{IR}$ was observed in the experimental group whereas a 19.7% increase was observed in control group. The difference between the

**Table 3 Changes in anthropometric parameters after 6 months on diet**

| | Units | Experimental group ($n$ = 30) | Control group ($n$ = 33) | Comparison of groups |
|---|---|---|---|---|
| *Weight loss* | | | | |
| | (kg) | 11.6 ± 0.84* | 9.06 ± 0.84* | $P$ = 0.024 |
| | (%) | 11.7 ± 0.66* | 9.96 ± 0.79* | $P$ = 0.053 |
| *BMI reduction* | | | | |
| Original | ($g/m^2$) | 3.99 ± 0.24* | 3.16 ± 0.27* | |
| Adjusted for baseline differences | ($g/m^2$) | 3.85 ± 0.25* | 3.28 ± 0.24* | $P$ = 0.115 |
| | (%) | 11.7 ± 0.66* | 9.68 ± 0.79* | $P$ = 0.053 |
| *Abdominal circumference decrease* | | | | |
| Original | (cm) | 11.7 ± 0.89* | 9.39 ± 0.98* | |
| Adjusted for baseline differences | (cm) | 11.1 ± 0.92* | 10.0 ± 0.88* | $P$ = 0.408 |
| | (%) | 10.5 ± 0.70* | 8.80 ± 0.90* | $P$ = 0.159 |
| *Body fat percent reduction* | | | | |
| Absolute | (%) | 6.98 ± 0.95* | 5.13 ± 0.59* | $P$ = 0.710 |
| Relative | (%) | 18.1 ± 2.45* | 14.1 ± 1.71* | $P$ = 0.122 |

Mean ± s.e. Analysis by two-factor ANOVA.
*Significant difference from day 0 ($P < 0.0001$).

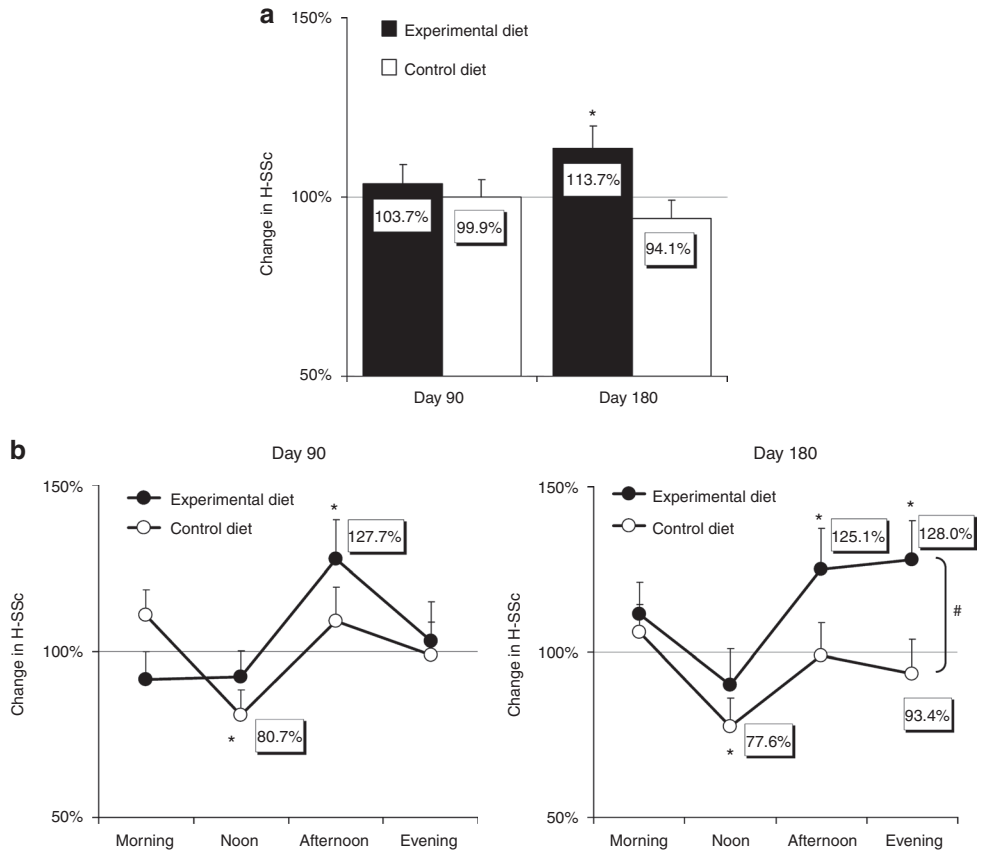


**Figure 2** Hunger and satiety scales. (**a**) Least square mean ± s.e. hunger-satiety scores (H-SSc) on day 90 and day 180 as a percentage of baseline (average daily satiety on day 0 and 7) in the experimental ($n$ = 18) and the control ($n$ = 21) groups. Comparison of groups by repeated measures ANOVA. *$P < 0.05$ for difference from baseline. (**b**) Mean ± s.e. percent of H-SSc at day 90 and at day 180 compared to scores at parallel hours on the first week of the diet (average day 0 and day 7). *$P < 0.05$ as compared to the same hour in the first week. #$P$ = 0.030 comparing control and experimental groups by contrast $t$-test following repeated measures ANOVA at day 180.

**Table 4 Biochemical and inflammatory parameters and percent of baseline**

| | | Experimental group ($n$ = 18) | | Control group ($n$ = 21) | | |
|---|---|---|---|---|---|---|
| | Day | Absolute mean | % of baseline[a] | Absolute mean | % of baseline[a] | Comparison of groups |
| Insulin (μU/ml) | 0 | 29.8 ± 5.52 | | 23.2 ± 4.48 | | |
| | 90 | 16.1 ± 1.93 | 84.4 ± 13.7 | 20.0 ± 3.61 | 102.9 ± 13.1 | $P$ = 0.332 |
| | 180 | 14.9 ± 2.79 | 68.0 ± 14.3* | 16.6 ± 1.63 | 122.6 ± 12.8 | $P$ = 0.006 |
| Glucose (mmol/l) | 0 | 5.10 ± 0.26 | | 4.85 ± 0.25 | | |
| | 90 | 4.81 ± 0.15 | 88.6 ± 8.35 | 4.77 ± 0.08 | 96.7 ± 6.84 | $P$ = 0.454 |
| | 180 | 4.71 ± 0.18 | 80.0 ± 7.53** | 4.71 ± 0.16 | 93.7 ± 6.84 | $P$ = 0.184 |
| $HOMA_{IR}$ | 0 | 1.68 ± 0.24 | | 1.33 ± 0.20 | | |
| | 90 | 1.14 ± 0.15 | 69.1 ± 15.8 | 1.33 ± 0.16 | 119.7 ± 12.8 | $P$ = 0.015 |
| | 180 | 1.09 ± 0.12 | 89.0 ± 15.2 | 1.20 ± 0.15 | 121.3 ± 13.2 | $P$ = 0.114 |
| Triglycerides (mmol/l) | 0 | 1.88 ± 0.17 | | 2.00 ± 0.17 | | |
| | 90 | 1.22 ± 0.09 | 69.2 ± 7.20*** | 1.22 ± 0.14 | 65.8 ± 5.92*** | $P$ = 0.717 |
| | 180 | 1.20 ± 0.13 | 70.6 ± 6.95*** | 1.33 ± 0.17 | 68.7 ± 6.00*** | $P$ = 0.834 |
| Total cholesterol (mmol/l) | 0 | 5.46 ± 0.18 | | 5.02 ± 0.15 | | |
| | 90 | 4.94 ± 0.17 | 91.9 ± 2.63** | 4.76 ± 0.18 | 95.7 ± 2.45 | $P$ = 0.290 |
| | 180 | 5.32 ± 0.23 | 97.6 ± 2.75 | 4.87 ± 0.18 | 96.3 ± 2.48 | $P$ = 0.733 |
| LDL-cholesterol (mmol/l) | 0 | 3.66 ± 0.18 | | 3.14 ± 0.15 | | |
| | 90 | 3.29 ± 0.18 | 89.0 ± 3.52** | 3.18 ± 0.15 | 97.8 ± 3.28 | $P$ = 0.073 |
| | 180 | 3.43 ± 0.22 | 90.3 ± 3.70* | 3.00 ± 0.13 | 92.4 ± 3.26* | $P$ = 0.670 |
| HDL-cholesterol (mmol/l) | 0 | 0.78 ± 0.06 | | 0.83 ± 0.05 | | |
| | 90 | 0.88 ± 0.04 | 114.3 ± 4.48** | 0.91 ± 0.04 | 110.4 ± 4.18* | $P$ = 0.525 |
| | 180 | 1.07 ± 0.09 | 140.8 ± 4.65*** | 1.05 ± 0.05 | 126.0 ± 4.16** | $P$ = 0.022 |
| CRP (mg/l) | 0 | 8.2 ± 2.0 | | 3.4 ± 0.6 | | |
| | 90 | 5.6 ± 1.6 | 99.0 ± 19.8[b] | 2.5 ± 0.4 | 98.3 ± 19.1[b] | $P$ = 0.979 |
| | 180 | 3.9 ± 1.1 | 72.2 ± 20.8[b] | 2.2 ± 0.4 | 94.2 ± 19.5[b] | $P$ = 0.456 |
| TNF-α (pg/ml) | 0 | 1.89 ± 0.15 | | 1.93 ± 0.24 | | |
| | 90 | 1.85 ± 0.18 | 101.4 ± 8.39 | 2.14 ± 0.29 | 117.3 ± 7.80* | $P$ = 0.169 |
| | 180 | 1.65 ± 0.16 | 90.8 ± 8.82 | 2.12 ± 0.33 | 116.2 ± 7.78* | $P$ = 0.034 |
| IL-6 (pg/ml) | 0 | 2.71 ± 0.33 | | 2.52 ± 0.26 | | |
| | 90 | 2.22 ± 0.33 | 84.8 ± 13.4 | 2.06 ± 0.27 | 91.5 ± 11.9 | $P$ = 0.710 |
| | 180 | 1.61 ± 0.21 | 63.0 ± 13.4** | 1.84 ± 0.20 | 76.3 ± 12.2 | $P$ = 0.465 |

Least squares mean ± s.e. for absolute values and percent of baseline. Insulin, glucose, $HOMA_{IR}$, triglycerides, CRP, TNF-α, and IL-6 were calculated as percent from day 0. Total cholesterol, LDL-cholesterol and HDL-cholesterol were calculated as percent from days 0 and 7. To convert values for glucose, triglycerides, total cholesterol, LDL-cholesterol and HDL-cholesterol to mg/dl, divide by 0.05551, 0.01129, 0.02586, 0.02564, and 0.02564, respectively.
CRP, C-reactive protein; HDL, high-density lipoprotein; $HOMA_{IR}$, homeostasis model assessment for insulin resistance; IL-6, interleukin-6; LDL, low-density lipoprotein; TNF-α, tumor necrosis factor-α.
[a]Percentages of baseline values were calculated for each subject and averaged. [b]Adjusted for baseline differences.
*, **, ***Significant difference from baseline ($P$ < 0.05, $P$ < 0.01, $P$ < 0.0001, respectively).

groups was significant ($P$ = 0.015). A similar trend was found on day 180 (11.0% decrease vs. 21.3% increase respectively). Both diets led to a significant reduction in morning fasting triglyceride concentrations compared to baseline at day 90 and 180 (30.8 and 34.2%, at day 90, respectively, 29.4 and 31.3% at day 180, respectively, $P$ < 0.0001). The experimental diet led to 8.1% significant decrease in total cholesterol concentrations ($P$ < 0.01), whereas only a 4.3% decrease was observed in the control on day 90. The effect was not observed on day 180. An earlier and significant decrease of 11.0% in LDL-cholesterol concentrations was found in the experimental group on day 90 ($P$ < 0.01) whereas on day 180 a significant decrease in LDL-cholesterol was measured for both diets (9.7 and 7.6% decreases respectively, $P$ < 0.05). Significant increases in HDL-cholesterol concentrations were observed for both diets on day 90 and 180 (14.3%, $P$ < 0.01 vs. 10.4%, $P$ < 0.05 at day 90 and 40.8%, $P$ < 0.0001 vs. 26.0%, $P$ < 0.01 at day 180). The experimental diet HDL-cholesterol increase was significantly greater compared to the control diet increase after 180 days ($P$ = 0.022).

### Serum inflammatory parameters level

Measurements of inflammatory markers are shown in Table 4. A trend of a greater CRP reduction was observed in the experimental group (27.8 vs. 5.8%). Significant differences were not achieved after adjusting for baseline differences. On day 180, subjects on the experimental diet had significantly lower TNF-α concentration, with a 9.2% decrease from baseline measurements. In contrast, the control diet led to a 16.1% increase in TNF-α ($P = 0.034$ for difference between groups). Both diets lowered IL-6 concentrations at day 90 and 180 compared to baseline. At day 180, the experimental diet led to a significant reduction of 37.8% ($P < 0.01$) whereas a smaller insignificant reduction of 23.7% was found in the control diet. On day 90 a similar trend was observed (15.8% vs. 10% reduction from baseline, respectively).

### Serum hormonal levels

Both diets decreased average 12-h leptin concentrations on day 90 and day 180 compared to baseline ($P < 0.05$) (Figure 3a).

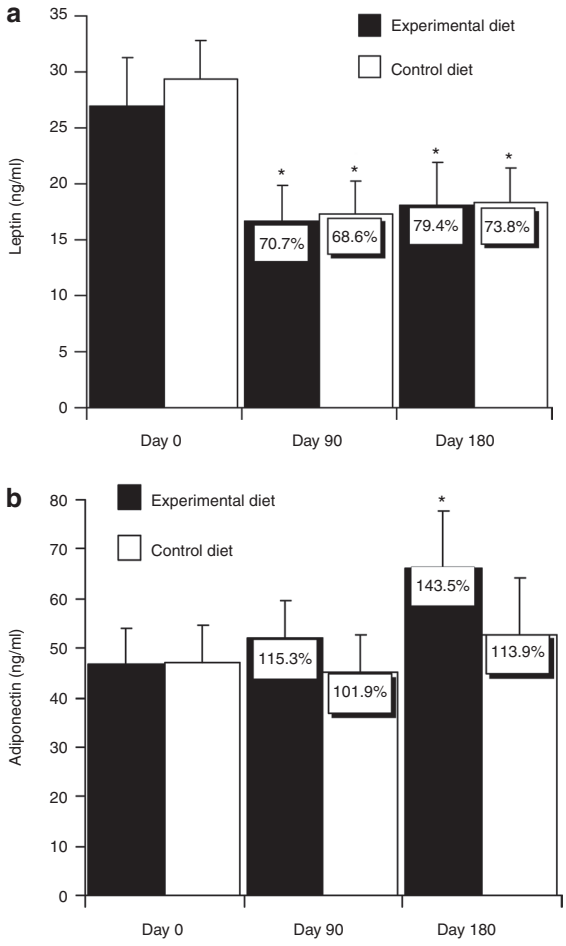


**Figure 3** Mean ± s.e. for absolute values, least squares mean for percentage of baseline (shown in boxes on bars) in the experimental ($n = 18$) and the control ($n = 21$) groups. Average daily (**a**) leptin and (**b**) adiponectin at days 0, 90, and 180. Comparison of groups for percentages of baseline by repeated measures ANOVA. *$P < 0.05$ for difference from baseline by *t*-test using standard errors from ANOVA. Percentage of baseline values were calculated for each subject and averaged.

A trend to smaller reductions from baseline was observed in the experimental group (29.3 and 20.6% decrease in the experimental group, respectively, 31.4 and 26.2% decrease in the control group, respectively).

The experimental diet led to a significant increase (43.5%, $P < 0.05$) in average 12-h adiponectin concentrations, whereas the control diet led to a smaller and insignificant (13.9%) increase after 180 days (Figure 3b). The same trend was observed on day 90 (15.3 vs. 1.9%, respectively).

## DISCUSSION

This randomized clinical trial, performed in a sample of police officers with BMI >30, examined the effects of a low-calorie diet based on carbohydrates eaten mostly at dinner, in comparison to an identical low-calorie diet providing carbohydrates throughout the day.

Greater weight loss, abdominal circumference, and body fat mass reductions were observed in the experimental diet in comparison to controls (Table 3). The experimental diet group's H-SScs were higher in comparison to baseline (Figure 2). After 180 days, a drop in averaged 12-h leptin concentrations was observed in both diet groups. A trend to smaller reduction in averaged 12-h leptin concentrations from baseline was observed in the experimental group (Figure 3a). The decrease observed in overall daily leptin concentrations for both groups has been documented in previous studies (2,14–16) and may be explained by reduced body fat mass (Table 3). Reduced levels of leptin during weight loss programs is commonly associated with a decline in satiety levels (14,15) as was observed in our control group. In the experimental group, this expected satiety reduction did not occur. On the contrary, at the end of the study, the experimental diet group had higher H-SSc in comparison to baseline.

It is proposed that the smaller reduction in averaged 12-h leptin concentration, induced by the experimental diet, may be an important factor in the higher levels of satiety reported during the day. Previous studies with different diets reported that during weight loss, leptin concentrations decreased, satiety levels were reduced, food intake renewed and a slow regain of body weight occurred (14,15,17). Thus, dietary manipulations that will maintain higher daytime leptin concentrations during daylight hours in weight loss process may be beneficial. Our experimental diet might manipulate daily leptin secretion, leading to higher relative concentrations throughout the day. We propose that this modification of hormone secretion helped participants experience greater satiety during waking hours, enhance diet maintenance over time and have better anthropometric outcomes.

Although, no specific nutritional guidance regarding glucose balance, lipids profiles or inflammation status was given to participants, improvements in these parameters were observed. It is of great interest that for nearly all of these parameters, significantly greater improvements were observed in the experimental diet group (Table 4). Significantly higher improvements of glucose balance and insulin resistance ($HOMA_{IR}$), lipid profile (total cholesterol, LDL-cholesterol, HDL-cholesterol) and the

inflammation markers (CRP, TNF-α, IL-6) were measured in the experimental group. A significant increase in average 12-h adiponectin concentrations, was observed at the end of the study in the experimental group only (**Figure 3b**), even though both diet groups experienced weight loss accompanied by body fat and abdominal circumference reductions (**Table 3**).

It is known that adiponectin is negatively associated with plasma insulin (11,18). Despite being secreted from the adipose tissue, plasma adiponectin concentrations are decreased in obesity (18). However, studies dealing with weight loss diets, report variable results including increased, decreased or unchanged plasma adiponectin levels (19–24). It has been suggested that mechanisms related to obesity-induced insulin resistance are the causes for low concentrations of adiponectin in obesity. It has also been speculated that hypo-adiponectinemia can be reversed only by a weight reduction process, which reverses adipose tissue-specific insulin sensitivity (25–27). Accordingly, the rise in adiponectin concentrations during weight loss depends on the type of diet administered. Our experimental diet led to lower insulin concentrations during daylight hours and improved insulin resistance as seen in $HOMA_{IR}$ results (**Table 4**) and therefore, we believe, increased adiponectin concentrations more than the control.

Previous studies found that in obesity (primarily abdominal), adiponectin concentrations are low, insulin resistance is high, the risk for type 2 diabetes increases, an atherogenic lipid profile evolves, and a high concentration of several inflammatory markers appears (CRP, TNF-α, IL-6) (6,23,27,28). It is well established that losing weight, especially from abdominal fat stores, increases adiponectin concentration and improves all these parameters since adiponectin is insulin sensitizing, directly reduces metabolic and vascular disorders and acts as an anti-inflammatory adipokine (27,28). In insulin resistant mice treated with physiologic concentrations of adiponectin, glucose tolerance improved and insulin resistance was reduced (29). It has also been found that when lean mice were given injections of adiponectin with a high-fat, high-sugar diet, postprandial increases in plasma glucose, free fatty acid and triacylglycerol concentrations were lower (29). Our findings indicate that consuming carbohydrates mostly at dinner increases adiponectin levels, in comparison to the standard control diet, leading to improvements in insulin resistance, the metabolic syndrome profile, and inflammatory status.

Overall, we have demonstrated improvement in hunger/satiety status, persistence in the weight loss process, better anthropometric outcomes, improved insulin sensitivity, improvement in metabolic syndrome parameters, less inflammation and hormonal changes, following simple carbohydrate manipulation. Our results provide a scientific basis for proposing possible dietary alternatives that may be beneficial for people suffering from obesity, insulin resistance, and the metabolic syndrome and experiencing difficulties in maintaining a weight loss diet over the long term. Further research is required to confirm and clarify the mechanisms by which this relatively simple diet approach enhances satiety, leads to better anthropometric outcomes, and achieves improved metabolic response, compared to a more conventional dietary approach.

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## DISCLOSURE

The authors declared no conflict of interest.



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