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Changes in daily leptin, ghrelin and adiponectin profiles following a diet with carbohydrates eaten at dinner in obese subjects

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Abstract *Background and aims:* Our recently published randomised clinical trial evaluated the effect of a low-calorie diet with carbohydrates eaten at dinner. This dietary pattern led to lower hunger scores, and better anthropometric, biochemical and inflammatory outcomes compared to a standard low-calorie diet. In the same study, changes in diurnal secretion patterns of leptin, ghrelin and adiponectin were investigated.
Methods and results: Seventy-eight police officers (body mass index (BMI) > 30) were randomly allocated to experimental (carbohydrates at dinner) or control weight loss diets for 6 months. Sixty-three subjects finished the programme. On days 0, 7, 90 and 180 blood samples and hunger scores were collected every 4 h from 8:00 to 20:00. Hormonal profiles were available for 39.

The dietary manipulation led to changes in daylight hormonal profiles in the experimental group. Leptin's secretion curve became convex, with a nadir later in the day (significant difference compared to baseline at morning and evening, $p = 0.023$, $p = 0.021$, respectively). Ghrelin's secretion curve became concave, peaking only in the evening hours. Adiponectin's curve was elevated only after the experimental diet (significant difference compared to baseline at afternoon, $p = 0.044$).
Conclusions: We propose that a low-calorie diet with carbohydrates eaten at dinner can modulate daytime hormonal profiles. Taken together with our earlier results, we believe this diet regime

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may prevent mid-day hunger, better support weight loss and improve metabolic outcomes compared to conventional weight loss diets.

The trial is registered at controlled-trials.com, ISRCTN37829376, December 2009.

Weight reduction is still considered to be one of the most effective methods for treatment of metabolic complications and cardiovascular risk associated with obesity [1,2]. Yet, most obese subjects are trapped in 'obesity's vicious cycle', fail to maintain long-term diets and regain body weight [3,4]. This phenomenon can be explained, at least in part, by the increased understanding of the metabolic role of adipose tissue. Adipose tissue is no longer considered exclusively an energy storage site for the body. Today, it is looked upon as an endocrine organ that synthesises and secretes adipocytokines that regulate hunger and satiety and impact the development of insulin resistance, the metabolic syndrome and inflammation [5].

Leptin provides information of adipose tissue status to receptors in the brain and regulates hunger, satiety and food intake [5,6]. Paradoxically, this 'satiety hormone' is at its highest levels during the late night hours when most individuals are asleep. Leptin levels fall during the day from 8:00 to 16:00, and start to increase from 16:00 reaching higher levels at night [7,8].

Ghrelin, produced in the stomach and not in the adipose tissue yet, is also related to energy balance. Ghrelin concentrations rise before meals and stimulate eating [6,9,10]. The secretory patterns of ghrelin, 'the hunger hormone', also appear to work against dieters as high values are maintained throughout the day with a zenith after 13:00 and low values appearing at night [8,11].

Adiponectin is considered to be 'the link between obesity, insulin resistance and the metabolic syndrome' [12–14]. Despite being secreted from the adipose tissue, plasma adiponectin concentrations are decreased when people gain fat mass, in particular, in the abdominal area [12,14]. In normal-weight subjects or overweight subjects who lose weight, a rise in adiponectin's diurnal curve is detected [8,15].

Our recently published study involved an innovative dietary regimen that led to increased satiety, achieved better anthropometric outcomes and improved insulin resistance, metabolic and inflammatory parameters compared to controls [16]. The current analyses investigated whether this dietary regimen is accompanied by changes in hormonal secretion patterns.

We hypothesised that consumption of carbohydrates, mostly in the evening, would modify the typical diurnal pattern of leptin secretion and lead to relatively higher mid-day levels similar to changes observed in Muslims during Ramadan [17,18]. We further propose that such a change in leptin's relative concentration may account for satiety enhancement during daylight hours and improved dietary adherence that were reported [16].

Since ghrelin's secretory pattern is reciprocal to leptin's, [19] it was hypothesised that the ghrelin diurnal pattern would also be inverted and that relatively lower concentrations in daylight hours would delay the initiation of hunger sensations and help participants adhere to their diet.

Considering the negative correlation between insulin and adiponectin [20], it was deemed possible that this experimental diet would lead to higher adiponectin curves throughout the day compared to controls. This would provide a biologically plausible explanation for the greater improvements in insulin resistance, attenuation of symptoms of the metabolic syndrome and diminished inflammation status that were observed when carbohydrate consumption was predominant in the evening hours [16].

Methods

Study population and procedures

The study protocols have been described previously [16]. Briefly, 78 police officers (men and women), aged 25–55, body mass index (BMI) > 30, who met study criteria (had no primary diseases and were not pregnant and did not follow any type of diet regimen within a year prior to the study), took part in the 6-month parallel group randomised clinical study. All participants signed informed consent forms (approved by the Regional Committee for Human Experimentation, Kaplan Hospital (Rehovot, Israel), in accordance with the Helsinki Declaration). Out of 78 subjects who met the inclusion criteria and were randomly allocated to the experimental or control diet groups, 63 subjects completed the programme. The difference in dropout rates between the groups was non-significant ($p = 0.39$). On day 0, participants met the project dietician, completed questionnaires, underwent anthropometric measurements and were then randomly assigned to the experimental or the control group. The experimental group was prescribed a standard low-calorie diet (20% protein, 30–35% fat, 45–50% carbohydrates, 1300–1500 kcal) providing carbohydrates mostly at dinner, while the control group received a standard low-calorie diet (20% protein, 30–35% fat, 45–50% carbohydrates, 1300–1500 kcal), providing carbohydrates throughout the day (Table 1). The dietician met all participants personally at 1–3-week intervals and on each of the study time points (4-daylong events), for anthropometric measurements and in order to perform a comprehensive inquiry and estimate adherence to dietary regimen. Participants who did not attend meetings with the dietician or did not adhere to their diet were excluded from the study. On days 0, 7, 90 and 180 blood samples and hunger scores were collected every 4 h before meals. A few policemen were on duty or called up for special assignments at each time point. Consequently, blood data were available for 39 subjects who participated in all four full-day events. A flow diagram of the study is presented in our previous paper [16].

Blood sampling and biochemical analyses

Fasting (12 h) blood samples were taken at 08:00 and in intervals of 4 h (at 12:00, 16:00 and 20:00) before meals on each analysis day. Blood was centrifuged ($400\times$ *g*) and serum was collected and stored at $-20\ ^{\circ}C$ for measurement of leptin, ghrelin (total) and adiponectin (high molecular