HORMONES 2013, 12(1):101-110

Research paper

Enhancing treatment of obesity by using a distracting mini-meal: a new approach to an old problem

Antonio Picarelli[1], Marco Di Tola[1], Fabio Tabacco[2], Mariacatia Marino[1], Raffaele Borghini[1], Tania D'Amico[3], Carla Lubrano[3], Patrizia Gargiulo[3]

[1]Department of Internal Medicine and Medical Specialties, Sapienza University, [2]UOC Laboratory Diagnostics, S. Andrea Hospital, [3]Department of Experimental Medicine, Sapienza University, Rome, Italy

ABSTRACT

OBJECTIVE: The management of obesity, apart from exercise, mainly involves a calorie restriction regimen. A pharmaceutical treatment is often used to improve patient compliance and diet effectiveness, although several side-effects have previously been described. To improve patient compliance and diet effectiveness without incurring unpleasant side-effects, we evaluated whether a distracting mini-meal can physiologically decrease the absorption of fats and carbohydrates. DESIGN: Two minutes before each of the three meals consumed daily, 32 obese patients were treated with a distracting mini-meal, 32 with metformin, and 32 with placebo. At baseline and after 1, 3, and 6 months of treatment, body weight, body mass index, waist circumference, fasting/post-prandial insulinaemia and glycaemia, homeostasis model assessment-index, triacylglycerols, and total cholesterol were evaluated. RESULTS: All patients showed good compliance. With the exception of post-prandial glycaemia, a significant reduction in all parameters was documented in every group, albeit the greater variation was observed in patients treated with a distracting mini-meal or metformin. No one showed noteworthy side-effects. CONCLUSIONS: Our study focuses on a distracting mini-meal that could become a useful tool in enhancing weight loss. The beneficial effect of a distracting meal on insulin resistance, glucose, and lipid metabolism suggest its possible use to prevent or mitigate obesity-related disorders.

Key words: Calorie restriction regimen, Distracting mini-meal, Metformin, Obesity, Pharmaceutical treatment

INTRODUCTION

The Western diet is currently characterized by a high-calorie and low-fiber alimentary pattern, so that the ability to store chemical energy from nutrients is being seriously undermined, this resulting in obesity.[1,2] Obesity is defined as an excess of body fat that more often than not leads to health damage.[3,4] Moreover, increasing evidence is showing that obesity is a condition both predisposing to and aggravating the course of other pathological conditions such as insulin resistance (IR), type 2 diabetes mellitus (T2DM), and a

Address for correspondence:
Antonio Picarelli, M.D., Department of Internal Medicine and Medical Specialties, Sapienza University - Polyclinic Umberto I, Viale del Policlinico, 155, 00161 - Rome, Italy, Tel.: +39649978370, Fax: +3964450219, e-mail: antonio.picarelli@uniroma1.it

Received 23-05-12, Accepted 21-08-12

number of medical disorders collectively known as the metabolic syndrome.[5-10]

The commonest therapeutic approach in the management of obesity entails a dietary regimen based on calorie restriction combined with lifestyle modifications. However, since dietary restrictions are usually not effective,[3] a pharmaceutical treatment is often prescribed to boost patient compliance and diet effectiveness.[11-13] Treatment with metformin, a dimethyl-biguanide mainly used as an insulin-sensitizing and anti-hyperglycaemic agent in patients with IR or T2DM,[14] produces beneficial outcomes on body weight[15,16] even though, in some cases, gastrointestinal adverse effects require discontinuation of the drug.[17] Even during treatment with orlistat, another drug that enhances weight reduction through inhibition of pancreas lipase activity and triacylglycerols absorption,[11] some side-effects, such as abdominal discomfort and diarrhoea, can easily occur.[18] In a nutshell, restriction of calories is the cornerstone of any weight reduction programme, although until now such treatment has often been unsatisfactory both for patient and practitioner.

In an effort to improve patient compliance and diet effectiveness without incurring the risk of unpleasant side-effects, we aimed to reduce the absorption of fats and carbohydrates in a physiological way. For this purpose, we evaluated whether a distracting mini-meal, carefully planned and administered orally just before each normal meal, might be able to physiologically decrease the efficiency of digestion and thus of the absorption process during a controlled dietary regimen.

SUBJECTS AND METHODOLOGY

Chemical preparations

An "A" soluble chemical formulation, named distracting mini-meal, was prepared with a monounsaturated fatty acid (oleic acid; 2 g), four essential amino acids (methionine, L-phenylalanine, tryptophan, and valine; 2.5 mg for each), and one sugar (D-dextrose; 6 g) for a total nutritional intake of 42.4 Kcal/dose (Bionatural srl, Rome, Italy).

A "B" soluble pharmaceutical preparation was made with 1 g of metformin (Merck Serono SpA, Rome, Italy). A "C" soluble placebo formulation was made up with a biologically inert powder (Bionatural srl).

Before use, each chemical preparation was dissolved in 150 mL of water containing a sufficient amount of citric acid to obtain a solution at pH 2.5.

Nutrients in the distracting mini-meal were used to appropriately stimulate the secretion, and thus the consumption of biliary and pancreatic juice, before the foods of the normal meal arrived in the duodenum. Metformin and placebo were used, respectively, as positive and negative control in relation to weight reduction and metabolic control. Prior to use, all chemical preparations were acidified up to pH 2.5 to stimulate the stomach functionality, and therefore to accelerate the gastric emptying.

Patients and treatment modality

The present study took shape from a parallel-arm design characterized, as follows, by three intervention arms performed on a total of 96 obese patients who, from January to December 2009, were referred consecutively to our Operative Unit.

Specifically, a series of 32 out-patients (11 male/21 female, mean age 39.6±12.3 years), called "group A" and presenting with slight-moderate obesity, were admitted to the study. All patients in this group were treated with a distracting mini-meal (solution A) in association with a controlled dietary regimen and were evaluated as the study population.

Another series of 32 out-patients (11 male/21 female, mean age 38.1±13.8 years), named "group B" and presenting with slight-moderate obesity, were enrolled. All patients in this group were treated with metformin (solution B) in combination with a controlled dietary regimen and were assessed as positive controls. Metformin was administered on account of the IR found in all patients belonging to this group.

A further series of 32 out-patients (11 male/21 female, mean age 37.8±15.7 years), called "group C" and presenting with slight-to-moderate obesity, were included in the study. All patients in this group were treated with placebo (solution C) in association with a controlled dietary regimen and were evaluated as negative controls.

Patients' inclusion criteria were: body mass index (BMI) ≥25 kg/m^2; waist circumference (WC) ≥94 cm in men and ≥80 cm in women. Patients' exclusion criteria were: age <18 and >65 years; lack of informed consent; presence of glucose intolerance, T1 or T2DM, and thyroid disorders.

Every chemical preparation was administered orally approximately 2 minutes before each of the three meals consumed daily (breakfast, lunch, and dinner). To ensure an adequate nutritional intake, each dietary regimen was implemented on the basis of daily calorie needs, calculated by the Harris and Benedict formula[19] including the baseline physical activity minus 200 Kcal. No physical training was prescribed so as not to interfere with the effects of the other treatments on weight loss and metabolism of both carbohydrates and lipids. All procedures followed in this study were in accordance with the ethical standards of the institutional committee responsible for human experimentation. Furthermore, informed consent was obtained from every patient being studied.

Monitoring of the patients under treatment

All patients taking part in the study and treated as above reported were regularly followed for 6 months.

Specifically, at different time-points (1, 3, and 6 months) from the beginning of each treatment, patient compliance was assessed by the careful examination of a patient's food diary followed, if needed, by a specific medical interview. Each study participant had kept the food diary for at least 7 consecutive days.

In order to evaluate the effectiveness of each treatment in enhancing weight loss, the body height, weight, and WC were measured, and thereafter BMI was calculated. The anthropometric measurements were performed by two trained observers. More specifically, the body height and weight were measured in the standing position by using a stadiometer (m) and a calibrated scale (kg), respectively. The WC was measured on exhalation phase obtained in the standing position by using a non-stretchable tape over the abdomen, midway between the lowest rib and the iliac crest (cm). The BMI was calculated as weight divided by the square of height (kg/m^2).

To investigate the effect of each treatment on IR and glucose metabolism, the fasting/post-prandial insulinaemia and glycaemia were determined by routine diagnostic methods. In brief, at the beginning of the study and after 1, 3, and 6 months of treatment, two serum samples were collected from every patient. The first sample was obtained after fasting for at least 12 hours, while the second was collected 2 hrs after ingestion of a standard meal. In both serum specimens, insulin was measured by a sandwich, enzyme-labeled chemiluminescent immunoassay on the automated analyzer UniCel DxI 800 (Beckman Coulter Inc., Fullerton, CA). In the same serum samples, glucose was measured by an enzyme colorimetric assay on the automated instrument Cobas Integra 800 (Roche Diagnostics, Indianapolis, IN). The homeostasis model assessment-index (HOMA-I) was used to better evaluate IR and glucose metabolism. HOMA-I was calculated as follows, in accordance with Matthews et al:[20]

$$\text{HOMA-I} = \text{Fasting insulinaemia } (\mu\text{IU/mL}) \times \text{Fasting glycaemia (mg/dL)} / 22.5$$

To study the impact of each treatment on lipid metabolism, triacylglycerols and total cholesterol were measured by routine diagnostic methods. Briefly, in serum specimens obtained after fasting for at least 12 hours, both triacylglycerols and total cholesterol were measured by an enzyme colorimetric assay via the Cobas Integra 800 system.

Finally, to evaluate the occurrence of side-effects resulting from any administered treatment, assessment was made of the clinical status with particular attention to episodes of asthenia and gastrointestinal discomfort, number of daily evacuations, daily faecal weight, and iron parameters including haemoglobin, serum iron, ferritin, and transferrin. In whole blood specimens collected in tubes with EDTA anticoagulant, haemoglobin was measured by haemochromocytometric assay on the automated cytometer ADVIA 2120 (Siemens Healthcare Diagnostics, Deerfield, IL). In serum samples, the concentrations of iron, ferritin, and transferrin were determined by routine diagnostic methods. In brief, iron was determined by a colorimetric assay performed via the Cobas Integra 800 system, ferritin was measured by a sandwich, enzyme-labeled chemiluminescent immunoassay via the UniCel DxI 800 system, and transferrin was quantified by an immunoturbidimetric assay via the Cobas Integra 800 system.

Concerning all serological determinations carried out in this study, the haemolyzed, icteric, lipemic, or grossly contaminated samples were avoided to ensure the achievement of correct results. For the same purpose, all diagnostic methods and analytical instruments used in this study were constantly monitored by means of both internal and external quality assessment (IQA and EQA) programs.

The mean clinical and metabolic data of the patients at the start of the study are summarized in Tables 1 and 2, respectively. From a first analysis, the absence of statistically significant differences among age, body weight, BMI, and WC measured or deduced in the different groups of patients (Table 1) indicates a good clinical match among the participants selected for this study. Conversely, the presence of statistically significant differences among metabolic parameters measured or deduced in the different groups of patients (Table 2) reflects the high variability of laboratory data from patient to patient. The latter finding could constitute a limitation to this and other similar studies.

Statistical analysis

In tables, all data were expressed as mean value ± standard deviation, while in figures, all parameter values were reported as median, quartile cutpoints (first and third quartile), and range (minimum and maximum value).

Table 1. Clinical data of the patients at beginning of study

	Group A	Group B	Group C
Number of patients	32	32	32
Gender (M/F)	11/21	11/21	11/21
Age (yrs)*	39.60±12.30	38.10±13.80	37.80±15.70
Body weight (kg)°	99.81±4.54	97.83±3.82	97.42±10.32
BMI (kg/m^2)†	34.04±1.81	33.08±2.30	34.26±3.58
WC (cm)‡	109.21±10.04	107.15±10.74	110.95±12.15
Specific treatment	Distracting mini-meal	Metformin	Placebo
Basic treatment	Controlled dietary regimen	Controlled dietary regimen	Controlled dietary regimen

Age, body weight, BMI, and WC data are expressed as mean value ± standard deviation. The symbols refer to one-way ANOVA calculated as first test among values of each parameter measured or deduced in the different groups of patients (inter-patient analysis). No post test has been performed. Every controlled dietary regimen refers to daily calorie needs, calculated by Harris and Benedict formula, minus 200 Kcal. Legend: BMI, body mass index; WC, waist circumference.
* overall p = 0.8590 (ns); ° overall p = 0.3356 (ns); † overall p = 0.1779 (ns); ‡ overall p = 0.3890 (ns).

Table 2. Metabolic data of the patients at beginning of study

	Group A	Group B	Group C	Overall p
Fasting insulinaemia (μIU/mL)	28.88±6.04*	32.20±2.17†	29.53±3.09	0.0093
Post-prandial insulinaemia (μIU/mL)	126.65±16.42°†	109.25±13.50	117.34±6.99	<0.0001
Fasting glycaemia (mg/dL)	89.44±4.50°§	82.38±5.22†	77.97±3.77	<0.0001
Post-prandial glycaemia (mg/dL)	120.88±2.94°	106.78±5.30§	117.94±3.63	<0.0001
HOMA-I	6.37±1.40†	6.54±0.58‡	5.69±0.73	0.0016
Triacylglycerols (mg/dL)	231.00±34.70†	231.70±8.40†	200.00±54.30	<0.0001
Total cholesterol (mg/dL)	321.80±52.90*	294.20±7.80	312.40±22.90	0.0050

All metabolic data are expressed as mean value ± standard deviation. The overall p refers to one-way ANOVA computed as first test among values of each parameter measured or deduced in the different groups of patients, while the symbols refer to Bonferroni's multiple comparison calculated as post test among the same values (inter-patient analysis). HOMA-I refers to the formula: Fasting insulinaemia (μIU/mL) × Fasting glycaemia (mg/dL) / 22.5. Legend: HOMA-I, homeostasis model assessment-index.
* p <0.05 vs. Group B; ° p <0.001 vs. Group B; † p <0.05 vs. Group C; ‡ p <0.01 vs. Group C; § p <0.001 vs. Group C.

Data achieved in this study were firstly analyzed by the Kolmogorov-Smirnov test to verify the normal distribution hypothesis within each statistical sample. Since the resulting p values were not significant ($p > 0.05$), it is reasonable to assume that data obtained from every group of patients fall into a Gaussian distribution, and they therefore were processed by means of parametric tests. In detail, the comparison among values of each parameter measured or deduced in the different groups of patients (inter-patient analysis) was performed by using the one-way analysis of variance (ANOVA) as the first test, for which the homoscedasticity assumption was confirmed by Bartlett's test for equal variances. If the overall p was ≤ 0.05, Bonferroni's multiple comparison was used as the post test. Within each group of patients, the comparison among values of each parameter measured or deduced at different time-points (intra-patient analysis) was performed by using the repeated measures ANOVA as the first test, for which the pairing effectiveness was opportunely verified. If the overall p was ≤ 0.05, Bonferroni's multiple comparison was used as the post test. For every test applied in this study, the p values ≤ 0.05 were considered significant.

All statistical evaluations were carried out by using the GraphPad Prism package (GraphPad Software Inc., San Diego, CA).

RESULTS

Patient compliance

At the end of the study as well as at its intermediate time-points, all patients under dietary treatment supplemented with the distracting mini-meal, metformin, or placebo showed good compliance.

Weight loss and effects on related parameters

After 6 months of treatment, a significant degree of weight loss was observed in each group of patients ($p < 0.001$ for each one). The mean weight loss was 16.7% in group A, 14.5% in group B, and 7.3% in group C. Consistently, in patients treated with the distracting mini-meal, the weight loss was significantly higher than in those taking metformin or placebo, while in patients treated with metformin, this parameter was significantly higher than in those taking placebo (Table 3).

A significant BMI decrement was noted in every group (Figure 1), although in patients treated with the distracting mini-meal, this reduction was higher than in those taking metformin in whom BMI lessening was superior to that in patients treated with placebo (Table 3).

A significant WC decrement was found in each group ($p < 0.01$ for Groups A and B; $p < 0.05$ for Group

Table 3. Parameter variations from the beginning of study to 6 months of treatment ($\Delta_{t0\text{-}t6}$)

	Distracting mini-meal	Metformin	Placebo	Overall p
Body weight (kg)	–16.71±2.54*‡	–14.18±3.86‡	–7.15±2.40	<0.0001
BMI (kg/m^2)	–5.70±1.00°‡	–4.48±1.51‡	–2.46±0.76	<0.0001
WC (cm)	–7.94±1.31†	–7.32±1.38†	–3.94±0.59	<0.0001
Fasting insulinaemia (μIU/mL)	–16.28±5.77‡	–19.81±4.05‡	–5.94±4.40	<0.0001
Post-prandial insulinaemia (μIU/mL)	–104.60±17.82*‡	–83.93±15.13‡	–43.25±7.75	<0.0001
Fasting glycaemia (mg/dL)	–4.88±5.86	–4.06±6.05	–2.00±5.36	0.1258 (ns)
Post-prandial glycaemia (mg/dL)	+1.27±5.24	–0.66±6.99	–0.34±6.38	0.4516 (ns)
HOMA-I	–3.75±1.36‡	–4.16±0.89‡	–1.26±0.91	<0.0001
Triacylglycerols (mg/dL)	–70.30±22.33†	–63.70±8.08†	–46.00±28.35	<0.0001
Total cholesterol (mg/dL)	–120.80±21.03*†	–91.20±8.85	–92.40±22.15	<0.0001

All $\Delta_{t0\text{-}t6}$ are expressed as mean value ± standard deviation. The overall p refers to one-way ANOVA computed as first test among values of each parameter measured or deduced in the different groups of patients, while the symbols refer to Bonferroni's multiple comparison calculated as post test among the same values (inter-patient analysis). For fasting/post-prandial glycaemia, no post test has been performed. Legend: BMI, body mass index; HOMA-I, homeostasis model assessment-index; WC, waist circumference.
* $p < 0.05$ vs. Metformin; ° $p < 0.01$ vs. Metformin; † $p < 0.05$ vs. Placebo; ‡ $p < 0.001$ vs. Placebo.

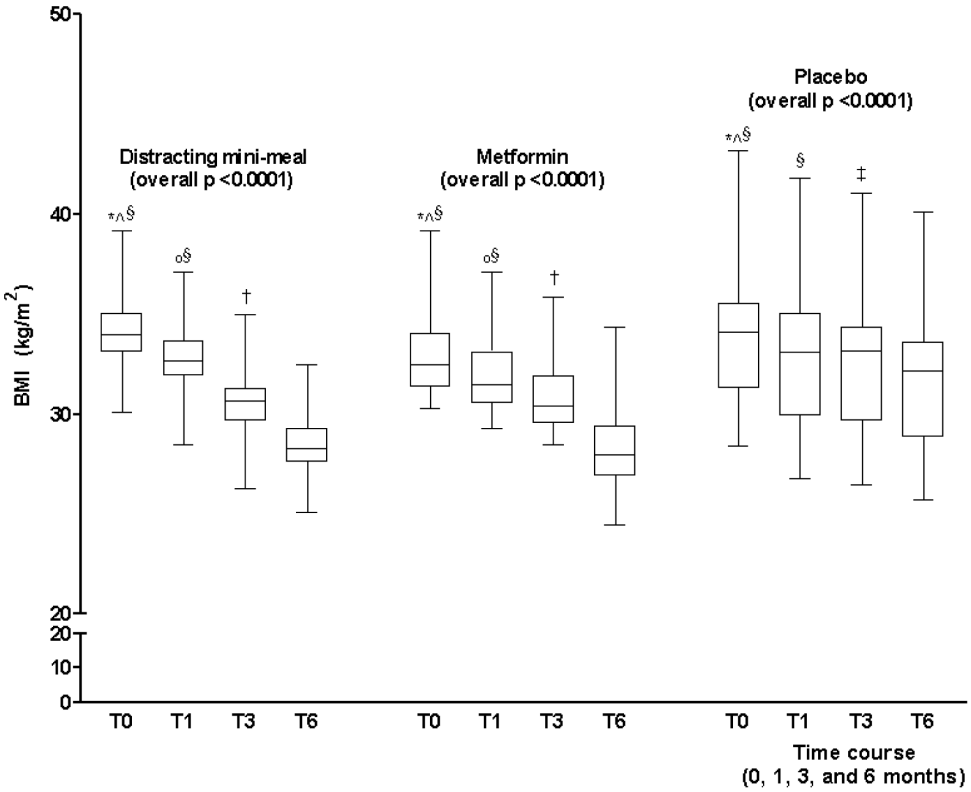

Figure 1. Box & whiskers plots (median, first and third quartile, minimum and maximum value) showing BMI changes at different time-points (1, 3, and 6 months) from the beginning of each treatment (distracting mini-meal, metformin, and placebo). The overall p refers to repeated measures ANOVA computed as first test among BMI values deduced in every group of patients at different time-points, while the symbols refer to Bonferroni's multiple comparison calculated as post test among the same values (intra-patient analysis). Legend: BMI, body mass index.
*** p** <0.05 vs. T1; ° p <0.05 vs. T3; ^ p <0.001 vs. T3; † p <0.05 vs. T6 ; ‡ p <0.01 vs. T6; § p <0.001 vs. T6.

C), although in patients treated with the distracting mini-meal or metformin this reduction was higher than in those taking placebo (Table 3).

Effects on insulin resistance and glucose metabolism

At the end of treatment, a significant decrement in fasting insulinaemia was observed in every group (p <0.001 for each one), although in patients taking the distracting mini-meal or placebo this parameter began to decrease only after the first month of treatment. The greater variation in fasting insulinaemia was particularly observed in patients treated with the distracting mini-meal or metformin, followed by those taking placebo (Table 3). A significant reduction in post-prandial insulinaemia was also observed in each group (p <0.001 for each one), although in all evaluated patients this parameter began to decrease only after the first month of treatment. The greater variation in post-prandial insulinaemia was especially noted in patients treated with the distracting mini-meal this followed, in decreasing order, by patients taking metformin and those treated with placebo (Table 3).

A significant decrement in fasting glycaemia was observed in every group (p <0.001 for Groups A and B; p <0.05 for Group C), although in patients taking the distracting mini-meal or metformin the fasting plasma glucose levels decreased during the first month and remained constant from the first to the sixth month of treatment, while in patients taking placebo this parameter began to decrease only after the third month of treatment. No statistically significant difference was detected among variations in fasting glycaemia deduced after each treatment (Table 3). In spite of the fluctuations in post-prandial glycaemia observed during the time course, no significant reduction was demonstrated in this parameter after

whichever treatment ($p > 0.05$ for each one).

A significant HOMA-I decrement was found in every group, albeit in patients taking distracting mini-meal or placebo this parameter began to decrease only after the third month of treatment (Figure 2). The greater HOMA-I variation was observed in patients treated with the distracting mini-meal or metformin, followed by those taking placebo (Table 3).

Effects on lipid metabolism

After 6 months of treatment, a significant reduction in triacylglycerols was highlighted in each group ($p < 0.05$ for each one), although in patients taking the distracting mini-meal or placebo this parameter decreased during the first month and remained constant from the first to the sixth month of treatment. The greater variation in triacylglycerols was observed in patients treated with the distracting mini-meal or metformin, followed by those taking placebo (Table 3).

A significant decrement in total cholesterol was clearly observed in every group ($p < 0.05$ for each one), although in patients taking metformin plasma levels of total cholesterol decreased during the first month and remained constant from the first to the sixth month of treatment, while in patients taking placebo this parameter began to decrease only after the first month of treatment. The greater variation in total cholesterol was observed in patients treated with distracting mini-meal, followed by those taking metformin or placebo (Table 3).

Side-effects

At the end of treatment, none of the patients taking part in the study showed gastrointestinal discomfort

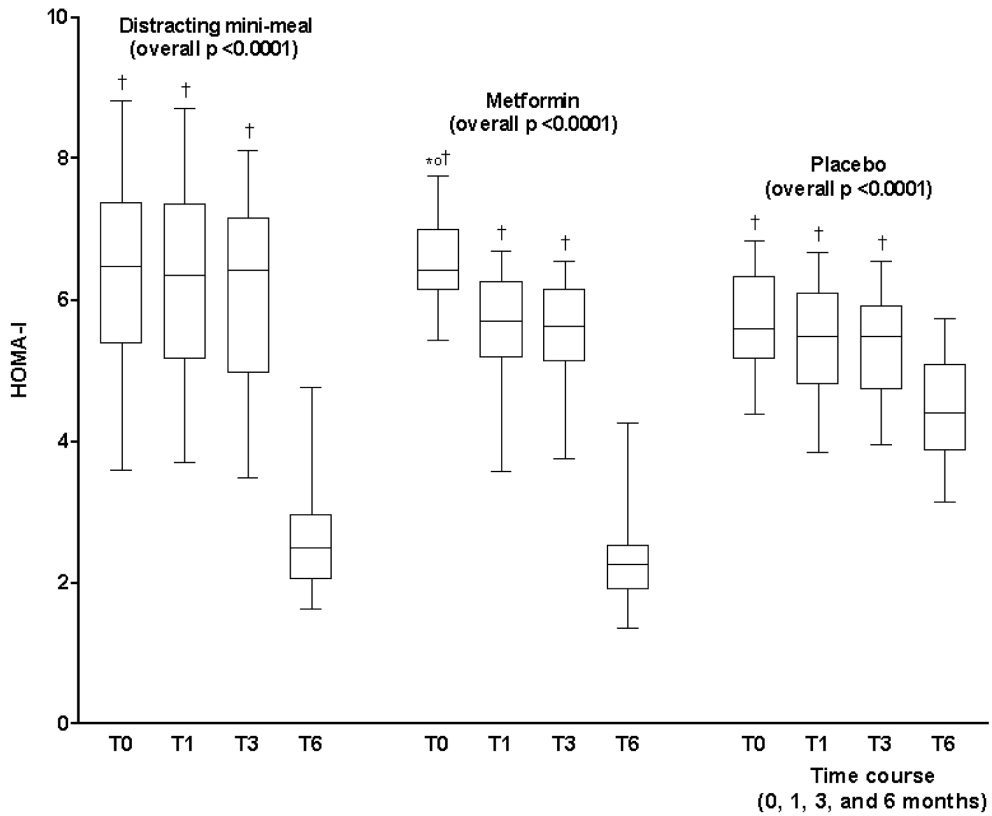

Figure 2. Box & whiskers plots (median, first and third quartile, minimum and maximum value) showing HOMA-I changes at different time-points (1, 3, and 6 months) from the beginning of each treatment (distracting mini-meal, metformin, and placebo). The overall p refers to repeated measures ANOVA computed as first test among HOMA-I values deduced in every group of patients at different time-points, while the symbols refer to Bonferroni's multiple comparison calculated as post test among the same values (intra-patient analysis). Legend: HOMA-I, homeostasis model assessment-index.
*** p** <0.01 vs. T1; ° p <0.001 vs. T3; † p <0.001 vs. T6.

except for an increase in the number of daily evacuations (9.4% of patients in group A, 6.3% in group B, and 3.1% in group C), though daily faecal weight remained constantly below the normal threshold (<200 g/24h). Furthermore, nobody showed asthenia, while the iron parameters, such as haemoglobin, were not significantly changed (13.4±1.5 vs. 12.8±1.3 g/dL in group A, 13.0±1.4 vs. 13.2±0.7 g/dL in group B, and 12.5±0.8 vs. 12.6±1.5 g/dL in group C).

DISCUSSION

The vast majority of authors agree that obesity, which is an excess of body fat, very often leads to health damage.[3,4] The limit beyond which the accumulation of fat assumes pathological significance has been fixed at ~20% of the ideal weight,[21] while the most accepted approach for treatment of obesity involves a calorie restriction regimen associated with appropriate physical exercise. This practice is based on a simple principle: if the supply of calories is less than the daily requirement, the reserves of fat are used for the energy balance up to their reduction. The corollary of such a strategy is the incorporation of physical exercise which, *per se*, is able to increase the expenditure of energy stored in the form of fat. However, bearing in mind that obesity is a chronic condition, the effectiveness of any dietary regimen is likely to be compromised by low compliance of patients.[3] A pharmaceutical supplement is often used to improve patient compliance,[11-13] though certain side-effects may necessitate discontinuation of the drug, for example, in patients treated with the dimethyl-biguanide metformin or the lipase inhibitor orlistat,[17,18] two drugs that produce favourable outcomes in body weight reduction.[11,15,16] Of note, although considerable progress has recently been made in this field, the therapeutic protocols for obesity are still unsatisfactory.

The main goal of our study was to offer an alternative approach to reducing the absorption of fats and carbohydrates in a physiological manner. For this purpose, we have developed a distracting mini-meal containing a fatty acid, four amino acids, and one sugar that are collectively able to induce an adequate secretion of digestive juice. Theoretically, the preemptive administration of the distracting mini-meal causes an initial secretion of biliary and pancreatic juice so that, when the normal meal arrives in the duodenum, the organism has no longer an enzymatic repertoire sufficient to digest all the foods ingested and the absorption of nutrients is thereby reduced. Our data firstly highlight the fact that obese patients treated with a distracting mini-meal, in association with a controlled dietary regimen, show good compliance. The main outcome of such treatment is an evident degree of weight loss, resulting in a significant decrement of both BMI and WC parameters. The greater effectiveness of a distracting mini-meal in determining weight loss versus metformin or dietary regimen alone moreover supports the hypothesis that the new treatment leads to a higher reduction in calories absorbed. Therefore, while the exact mechanism by which the distracting mini-meal leads to weight loss has yet to be elucidated, our data suggest that such treatment could to become a useful tool to improve both patient compliance and the effectiveness of any weight reduction programme.

Obesity is a condition predisposing to and aggravating the course of other pathological conditions including IR, T2DM, and the metabolic syndrome,[5-10] especially in cases with high abdominal fat distribution.[22,23] In this regard, our data show that treatment with a distracting mini-meal leads to a reduction in fasting/post-prandial insulinaemia, fasting glycaemia, and HOMA-I to an extent comparable to that obtained after treatment with metformin, an insulin-sensitizing and anti-hyperglycaemic agent mainly used in patients with IR or T2DM.[14] This outcome firstly confirms the hypothesis that the new treatment leads to a reduction in carbohydrate absorption. In agreement with previous studies showing that patients with acquired IR can recover the response to insulin after weight loss,[6] this finding also highlights a favourable effect of the new treatment for a reversal of the pathway that leads from obesity to IR, and eventually to T2DM. The reduction in visceral fat recorded after treatment with the distracting mini-meal contributes to its beneficial effect on the abovementioned pathway.

Another finding emerging from our study is the ability of the distracting mini-meal to lower total cholesterol to a greater extent than that obtained after treatment with metformin or dietary regimen alone. Furthermore, both the distracting mini-meal and metformin are able to lower triacylglycerols to

a greater extent than that obtained after treatment with a dietary regimen alone. These features fully confirm the capacity of the new treatment to reduce fat absorption as well as to exert a favourable effect on cardiometabolic risk factors associated with obesity.

Our data also show that in patients treated with the distracting mini-meal, no adverse effect is observable. The absence of unpleasant side-effects, including asthenia, gastrointestinal discomfort, increase in the number of daily evacuations and/or in daily faecal weight, and alterations of iron parameters, lends further support to the effectiveness and safety of using a distracting mini-meal in the management of targeted patients.

Among the strengths of our study is the fact that the distracting mini-meal could constitute a useful tool in the treatment of obese patients on account of its ability to determine weight loss. The new treatment is based on the possibility of misleading the absorption process through a "ghost meal" and therefore acts in a physiological fashion. This feature places the distracting mini-meal midway between a dietary regimen and any pharmaceutical treatment, ensuring both a favourable response and a good safety profile. Furthermore, just as a calorie restriction regimen is able to decrease the risk of several obesity-related disorders through modulation of IR and adipose tissue functions,[6,24] so the distracting mini-meal could also be used in the effort to prevent or mitigate the adverse outcomes of metabolic syndrome. Since a weakness of our study is the lack of evidence on the exact mechanism by which the distracting mini-meal leads to weight loss as well as to efficacious metabolic control, further investigations are needed to complete the pieces of this puzzle.

REFERENCES

1. Cordain L, Eaton SB, Sebastian A, et al, 2005 Origins and evolution of the Western diet: health implications for the 21st century. Am J Clin Nutr 81: 341-354.
2. James WP, 2008 The fundamental drivers of the obesity epidemic. Obes Rev 9: 6-13.
3. Kopelman PG, 2000 Obesity as a medical problem. Nature 404: 635-643.
4. Samper-Ternent R, Al Snih S, 2012 Obesity in older adults: epidemiology and implications for disability and disease. Rev Clin Gerontol 22: 10-34.
5. Erdmann J, Kallabis B, Oppel U, Sypchenko O, Wagenpfeil S, Schusdziarra V, 2008 Development of hyperinsulinemia and insulin resistance during the early stage of weight gain. Am J Physiol Endocrinol Metab 294: E568-575.
6. Ioannidis I, 2008 The road from obesity to type 2 diabetes. Angiology 59: 39S-43S.
7. Reaven GM, 1988 Banting lecture 1988. Role of insulin resistance in human disease. Diabetes 37: 1595-1607.
8. Park YS, Kim JS, 2012 Obesity phenotype and coronary heart disease risk as estimated by the Framingham risk score. J Korean Med Sci 27: 243-249.
9. Recio-Rodriguez JI, Gomez-Marcos MA, Patino-Alonso MC, et al, 2012 Abdominal obesity vs general obesity for identifying arterial stiffness, subclinical atherosclerosis and wave reflection in healthy, diabetics and hypertensive. BMC Cardiovasc Disord 12: 3.
10. Wietlisbach V, Marques-Vidal P, Kuulasmaa K, Karvanen J, Paccaud F, 2011 The relation of body mass index and abdominal adiposity with dyslipidemia in 27 general populations of the WHO MONICA Project. Nutr Metab Cardiovasc Dis [Epub ahead of print].
11. Mathys M, 2005 Pharmacologic agents for the treatment of obesity. Clin Geriatr Med 21: 735-746.
12. Palamara KL, Mogul HR, Peterson SJ, Frishman WH, 2006 Obesity: new perspectives and pharmacotherapies. Cardiol Rev 14: 238-258.
13. Bianchi C, Penno G, Romero F, Del Prato S, Miccoli R, 2007 Treating the metabolic syndrome. Expert Rev Cardiovasc Ther 5: 491-506.
14. Kuller LH, 2012 Metformin use among individuals at risk for type 2 diabetes. Curr Diab Rep 12: 265-273.
15. Meneghini LF, Orozco-Beltran D, Khunti K, et al, 2011 Weight beneficial treatments for type 2 diabetes. J Clin Endocrinol Metab 96: 3337-3353.
16. Yanovski JA, Krakoff J, Salaita CG, et al, 2011 Effects of metformin on body weight and body composition in obese insulin-resistant children: a randomized clinical trial. Diabetes 60: 477-485.
17. Florez H, Luo J, Castillo-Florez S, et al, 2010 Impact of metformin-induced gastrointestinal symptoms on quality of life and adherence in patients with type 2 diabetes. Postgrad Med 122: 112-120.
18. Johansson K, Neovius K, DeSantis SM, Rössner S, Neovius M, 2009 Discontinuation due to adverse events in randomized trials of orlistat, sibutramine and rimonabant: a meta-analysis. Obes Rev 10: 564-575.
19. Harris JA, Benedict FG, 1918 A biometric study of human basal metabolism. Proc Natl Acad Sci USA 4: 370-373.
20. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC, 1985 Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia 28: 412-419.
21. No authors listed, 2000 Obesity: preventing and managing the global epidemic. Report of a WHO consultation. World Health Organ Tech Rep Ser 894: 1-253.

22. Klein S, Allison DB, Heymsfield SB, et al, 2007 Waist circumference and cardiometabolic risk: a consensus statement from Shaping America's Health: Association for Weight Management and Obesity Prevention; NAASO, The Obesity Society; the American Society for Nutrition; and the American Diabetes Association. Diabetes Care 30: 1647-1652.
23. Jensen MD, 2008 Role of body fat distribution and the metabolic complications of obesity. J Clin Endocrinol Metab 93: S57-63.
24. Varady KA, Hellerstein MK, 2008 Do calorie restriction or alternate-day fasting regimens modulate adipose tissue physiology in a way that reduces chronic disease risk? Nutr Rev 66: 333-342.