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Original Article

Role of a proprietary mixture of water-soluble, viscous fibers and phytosterols in managing overweight/obese subjects poorly following a prescribed diet and physical exercise regimen. Preliminary results

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Summary: *Objective:* We evaluated the use of a mixture of water-soluble, viscous fibers and phytosterols/phytostanols (Fibermet®) in controlling body weight, body mass index, waistline, hip size, basal glycemia, post-prandial glycemia, cholesterol and triglycerides in overweight/obese subjects poorly adherent to follow a low-calorie diet and physical exercise regimen. *Methods:* Enrolled participants (N=50) were divided into a treatment and a control group. The treatment group (N=28) consisted of subjects poorly adherent to follow a low-calorie diet and prescribed physical exercise. The control group (N=22) consisted of subjects closely adherent to prescribed lifestyle changes. Anthropometric measurements and blood analysis were performed at enrolment and at the end of the study (T=28 days). *Results:* All 50 enrolled subjects completed the study. Subjects treated with Fibermet® significantly reduced their body weight and body mass index. Blood analysis revealed significant reductions of about 9% in post-prandial glycemia, total and LDL cholesterol, and triglycerides. Body weight and body mass index were also reduced in the control group (lifestyle intervention). No other parameters were modified by the intervention. *Conclusions:* Our results show that in subjects poorly adherent to hypocaloric diet and lifestyle changes, a mixture of water-soluble, viscous fibers together with phytosterols and phytostanols could help reduce overweight/obesity, post-prandial hyperglycemia and raised cholesterol and triglycerides.

Key words: psyllium, glucomannan, depolymerized guar gum, phytostanols

Introduction

The modern lifestyle, often characterized by a lack of physical activity as well as an unhealthy diet, has resulted in a worldwide rise in obesity, diabetes and atherosclerosis, currently the most prevalent and costly chronic diseases globally (1). Lifestyle changes and normalization of body weight (BW) are therefore required to prevent these conditions (2). Following a reduced calorie diet together with exercise results in significant and clinically meaningful weight loss, initially at least (3). However, high average dropout and lack of adherence to the prescribed therapy can result in failure (4). A preventive food approach aimed at decreasing the high glycemic index of meals and, consequently, hyperglycemia and hyperinsulinemia, could delay the development of insulin resistance and diabetes while also reducing overweight (5). Current evidence suggests that consuming slowly absorbed carbohydrates may also help maintain weight loss and hinder weight regain (6). Similarly, food substances capable of lowering cholesterol and triglyceride (TG) levels could reduce dyslipidemia, thus decreasing the risk of cardiovascular disease (7). Water-soluble fibers,

such as psyllium, glucomannan and depolymerized guar gum (DGG), are reported to reduce the glycemic index, hyperglycemia and hyperinsulinemia (8, 9). Moreover, due to their viscosity, they can act as bile sequestering agents, thus reducing cholesterol and TG levels (10). Finally, meta-analysis and systematic reviews have indicated that phytosterols and phytostanols, which compete chemically with cholesterol, could significantly decrease low density lipoprotein cholesterol (LDL-C), total cholesterol (TC) and TG levels (11, 12). We have therefore evaluated the clinical role played by a proprietary mixture of psyllium, glucomannan, DGG, phytosterols and phytostanols in controlling BW, body mass index (BMI), waistline (WL), hip size (HS), basal glycemia (BG), post-prandial glycemia (PPG), TC, LDL-C and TG in overweight/obese subjects poorly adherent to follow a low-calorie diet and physical exercise regimen. We have compared this group with a group of overweight/obese subjects adhering to prescribed lifestyle changes.

Patients and methods

Study criteria

A 4-week, open-label, controlled clinical trial was conducted in routine clinical practice, in accordance with the principles stated in the Declaration of Helsinki and consistent with Good Clinical Practice, as defined by the International Conference on Harmonization and in accordance with the ethical principles underlying European Union Directive 2001/20/EC and the United States Code of Federal Regulations, Title 21, Part 50 (21CFR50). The protocol and subject consent and privacy forms were approved by the review board before the study began. The trial was carried out in a single center in Italy between March and June 2016. A total of 50 overweight or obese (BMI: 27–41) Caucasian adults aged 20–65 years were enrolled. Exclusion criteria were: (1) blood pressure >170/100 mmHg; (2) glycated hemoglobin (HbA1c) >7%; (3) fasting blood TG >300 mg/dL; (4) TC >240; (5) previous myocardial infarction or stroke; (6) stage II/III/IV heart failure, or liver and/or renal disease; (7) need for thyroid hormone replacement therapy; (8) pregnancy or planning pregnancy; (9) excessive alcohol use; (10) self-reported current illicit drug/substance use; and (11) intolerance or allergy to any of the ingredients in the tested product. Every 7 days enrolled subjects reported their medical condition, specific study parameters such as tolerability and dosing compliance, and any side effects of treatment to the physicians responsible for the study. Subjects also were given daily access to the physicians if requested. All patients provided written informed consent to participate after they had received a full explanation of the study. All participants completed the study.

Study procedures

Participants (N=50) were divided into a treatment group and a control group. The treatment group (N=28) consisted of subjects previously declaring not to get to follow properly the low-calorie diet and physical exercise regimen proposed. The control group (N=22) consisted of subjects declaring to adhere closely the prescribed lifestyle changes. All outcomes were measured at enrolment and at the end of the study (T=28 days). Tolerability and side effects were noted regularly during the 28 days of the study, while compliance was reported at the end of the study.

Study objectives

The principal objectives of the study were: (1) clinical evaluation of the role played by a proprietary mixture of psyllium, glucomannan, DGG, phytosterols and phytostanols in controlling BW, BMI, WL, HS, BG, PPG, TC, LDL-C, HDL-C and TG in overweight/obese subjects; (2) clinical evaluation of the same parameters in subjects with a lifestyle intervention; and (3) evaluation of the safety and tolerability profiles of the tested product.

Tested product and treatment

The tested product was formulated in sachet form and contained a mixture of psyllium (1500 mg/dose), glucomannan (1000 mg/dose), DGG (500 mg/dose), phytosterols and phytostanols (ratio 95:5; 1500 mg/dose) and chromium (40 μg/dose). The product was manufac-

tured by S.I.I.T. (Trezzano S/N, Milan, Italy) and was notified to the Italian Ministry of Health as Fibermet® by Pharmextracta (Pontenure, PC, Italy), according to the provisions of law No. 169 of 2004, on September 15, 2015. The product was administered twice a day 5–10 min before the main meals of lunch and dinner with plenty of water.

Lifestyle intervention

The lifestyle intervention consisted of weekly individual sessions on nutritional education, reinforcement of exercise activity advice and peer group psychological support. A personal diary noting food consumption, daily physical activity and emotional reactions, was used as a tool for education and reinforcement. Daily caloric requirements were calculated using the Harris-Benedict equation and an individual activity factor. A diet based on a 500/1000 kcal/day deficit below the individual estimated caloric requirement was prescribed. The diet which was high in vegetables and low in salt and simple sugars, provided 20% of total energy intake as protein, 30% as fat and 50% as carbohydrates with a maximum cholesterol daily content of 300 mg/day. Fresh foods, with at least three fish meals per week, and avoidance of alcohol were recommended. The prescribed physical activity program consisted of 210 minutes per week of exercise including 70% moderate-intensity aerobic physical activity and 30% muscle-strengthening activity. The patient's dietary compliance and average weekly level of physical activity were recorded at each session. At the end of the 28-day lifestyle intervention, all participants were encouraged to continue with the same diet and physical activity program for succeeding months. Being totally (> than 85%) or poorly (< than 15%) adherent to the prescribed lifestyle interventions, tolerability and compliance were measured by questionnaire.

Measurements

Before starting the study, all patients underwent an initial screening assessment that included medical history, physical examination, vital signs (blood pressure and heart rate), measurement of height and BW, calculation of BMI, measurement of abdominal circumference (WL) and HS, and assessment of BG, PPG, TC, LDL-C, HDL-C, TG, aspartate aminotransferase (AST) and alanine aminotransferase (ALT). After 28 days of treatment, the following parameters were evaluated: BW, BMI, WL, HS, BG, PPG, TC, LDL-C, HDL-C, TG, AST and ALT. BMI was calculated as weight in kilograms divided by the square of height in meters. WL was measured midway between the lateral lower rib margin and the iliac crest with a Gulick anthropometric spring-loaded tape measure (Model 5829, Bell Medical Services, Neptune City, NJ, USA). Hip circumference was measured at the level of the trochanter.

Blood analysis

Blood samples were drawn by laboratory technicians, and assays were performed by the biologist in charge of the laboratory. All measurements were performed in a laboratory authorized by the Italian Ministry of Health.

Statistical analysis

The non-parametric Mann-Whitney test was used to compare differences between group outcomes during the same period. The non-parametric Wilcoxon signed rank test for matched pairs was used compare outcomes in the same group during different periods. The statistical software JMP 10 for Mac OsX was used and statistical significance was set at $P<0.05$.

Results

We examined the clinical role of a proprietary mixture of psyllium, glucomannan, DGG, phytosterols and phytostanols in controlling BW, BMI, WL, HS, BG, PPG, TC, LDL-C and TG in overweight/obese subjects (N=28) poorly adherent to follow a low-calorie diet and physical exercise regimen. Similar subjects declaring to closely adhere to a lifestyle intervention were enrolled in a control group (N=22) and did not received the product. All 50 enrolled subjects completed the study.

Table 1. Characteristics of participants (N=50) at enrolment

Treatment	Fibermet® (N=28)	Life style intervention (N=22)	p Value
Males/females	16/12	14/8	n.s.
Age (years)	49.5±11.3	51.6±9.4	n.s.

Values for age are expressed as the median ± standard deviation.
n.s., not significant.

As shown in Table 1, and also in second column of Table 4 (Δ%, T=0) the two groups were similar regarding age, sex, BW, BMI, WL, HS, BG, PPG, TC. LDL-C, HDL-C, TG, AST and ALT. As shown in Table 2, the subjects treated twice a day for 28 days with the water-soluble mixture of fibers plus phytosterols and phytostanols significantly reduced their BW by an average of more than 3 kg and their BMI by more than 5%. No significant differences were observed for WL or HS (reductions of 3.4 and 2.2 cm, respectively). Blood analysis revealed non-significant results for BG and HDL-C and significant results for PPG, TC, LDL-C and TG, with reductions of about 9%. On the other hand, the subjects adhering to the lifestyle intervention (Table 3) significantly reduced their BW and BMI by 5% and 8.5%, respectively. WL was also significantly reduced by 5 cm, while HS was non-significantly reduced by 2.7 cm. However, 28 days of lifestyle intervention did not significantly modify blood parameters.

Comparison of the results in the two groups at T=28 (Table 4) revealed significant differences, with product treatment having a greater effect than lifestyle intervention on PPG, TC, LDL-C and TG (reduced by 9.56%, 9.15%, 12.24% and 8.24%, respectively). No serious side effects were reported by the 28 treated subjects, although one of them reported a laxative-like effect, with moderate gastrointestinal discomfort. No side effects were reported by the 22 subjects accepting the lifestyle intervention (data not shown).

Table 2. Outcomes in subjects (N=28) treated for 28 days with Fibermet®

Parameter	T=0	T=28	Δ%	p Value
BW (kg)	97.9±9.5	94.7±7.2	-3.30%	<0.05
BMI (kg/m^2)	33.5±3.2	31.7±3.6	-5.40%	<0.05
WL (cm)	112.8±7.3	109.4±6.9	-3.00%	n.s.
HS (cm)	111.9±4.7	109.7±6.2	-2.00%	n.s.
BG (mg/dL)	112.5±10.3	109.6±8.7	-2.58%	n.s.
PPG (mg/dL)	129.2±10.8	118.3±6.9	-8.44%	<0.05
TC (mg/dL)	218.6±10.3	198.8±7.4	-9.06%	<0.05
LDL-C (mg/dL)	135.9±7.5	121.9±8.3	-9.40%	<0.05
HDL-C (mg/dL)	46.2±4.0	48.9±5.2	+5.80%	n.s.
TG (mg/dL)	173.6±18.9	158.2±15.6	-8.88%	<0.05
AST (U/I)	37.0±6.2	35.2±5.1	-5.87%	n.s.
ALT (U/I)	43.5±5.8	41.1±6.2	-5.50%	n.s.

Values are expressed as the median ± standard deviation.
ALT, alanine aminotransferase; AST, aspartate aminotransferase; BG, basal glycemia; BMI, body mass index; BW, body weight; HS, hip size; LDL-C, low density lipoprotein cholesterol; n.s., not significant; PPG, post-prandial glycemia; TC, total cholesterol; TG, triglycerides; WL, waistline.

Table 3. Outcomes in subjects (N=22) with lifestyle intervention

Parameter	T=0	T=28	Δ%	p Value
BW (kg)	98.5±10.3	93.6±8.8	-5.00%	<0.01
BMI (kg/m^2)	34.1±4.2	31.2±4.6	-8.50%	<0.01
WL (cm)	114.2±8.0	109.2±6.1	-4.40%	<0.05
HS (cm)	113.8±5.8	111.1±4.9	-2.70%	n.s.
BG (mg/dL)	114.0±10.5	108.2±9.0	-5.10%	n.s.
PPG (mg/dL)	131.1±8.5	130.8±8.3	-0.30%	n.s.
TC (mg/dL)	220.2±10.9	218.8±8.1	-0.60%	n.s.
LDL-C (mg/dL)	137.5±8.4	138.9±7.4	+1.00%	n.s.
HDL-C (mg/dL)	48.2±4.8	47.5±4.5	-1.50%	n.s.
TG (mg/dL)	169.8±15.1	172.4±10.9	+1.50%	n.s.
AST (U/I)	39.2±6.1	37.1±6.2	-4.40%	n.s.
ALT (U/I)	41.5±5.0	39.8±7.1	-4.10%	n.s.

Values are expressed as the median ± standard deviation.
ALT, alanine aminotransferase; AST, aspartate aminotransferase; BG, basal glycemia; BMI, body mass index; BW, body weight; HS, hip size; LDL-C, low density lipoprotein cholesterol; n.s., not significant; PPG, post-prandial glycemia; TC, total cholesterol; TG, triglycerides; WL, waistline.

Table 4. Fibermet® versus lifestyle outcomes at T=0 and T=28

	Δ%, T=0	p Value	Δ%, T=28	p Value
BW	-0.66%	n.s.	+1.17%	n.s.
BMI	-1.76%	n.s.	+1.60%	n.s.
WL	-1.23%	n.s.	+0.18%	n.s.
HS	-1.63%	n.s.	-1.27%	n.s.
BG	-1.06%	n.s.	-1.29%	n.s.
PPG	-1.45%	n.s.	-9.56%	<0.05
TC	-0.73%	n.s.	-9.15%	<0.05
LDL-C	-1.17%	n.s.	-12.24%	<0.01
HDL-C	-4.15%	n.s.	+2.95%	n.s.
TG	+2.23%	n.s.	-8.24%	<0.05
AST	-5.36%	n.s.	-5.13%	n.s.
ALT	+4.82%	n.s.	+3.27%	n.s.

Values are expressed as the median ± standard deviation.
ALT, alanine aminotransferase; AST, aspartate aminotransferase; BG, basal glycemia; BMI, body mass index; BW, body weight; HS, hip size; LDL-C, low density lipoprotein cholesterol; n.s., not significant; PPG, post-prandial glycemia; TC, total cholesterol; TG, triglycerides; WL, waistline.

Discussion

Following a hypocaloric diet and physical exercise regimen is surely the best approach for treating overweight, obesity, type 2 diabetes and, to a lesser extent, dyslipidemia, but is challenging for most people. Physical exercise requires time and can result in injury (13). Moreover, people are sometimes unable to maintain a hypocaloric diet due to commitments and stress, and often regain lost weight due to adaptive thermogenesis which frustrates their efforts (14, 15). However, water-soluble and viscous fibers expand in the stomach if taken with enough water, which could contribute to a partial reduction in appetite (16). Moreover, especially when in mixture, in both adults and in children/adolescents (17, 18), they help decrease overweight and obesity, reduce post-prandial hyperglycemia and insulin release, and lower levels of cholesterol and TG (19-22), even when administered as add-on therapy to statins (23). The cholesterol-lowering effect of water-soluble and viscous fibers, due to their bile salt sequestering ability (24, 25), can be augmented by mixing them with phytosterols and phytostanols. Their mechanism of action is mainly caused by the chemical competition inside lipid micelles between cholesterol and phytosterols/phytostanols (26).

The above may explain our findings whereby administration of a mixture of water-soluble, viscous fibers together with phytosterols/phytostanols slightly, but significantly, reduced BW and BMI in subjects poorly adhering to a hypocaloric diet or physical activity regimen. In these subjects, blood analysis revealed a reduction in post-prandial glycemia, likely due to the slowing absorption effect of the mixture of soluble and viscous fibers on blood sugars, and a considerable impact on lipidic profile, especially LDL-C ($p<0.01$). We observed good results regarding weight, BMI and WL in the control group but no effects on blood parameters, with no changes in glycemia, cholesterol and TG observed after 28 days of lifestyle intervention. Comparison of the results in the two different groups (treatment with fibers plus phytosterols and phytostanols or lifestyle intervention) indicates that the mixture of fibers and sterols is better at improving post-prandial glycemia, TC, LDL-C and TG. The reductions in BW and BMI in the two groups are too similar to allow a statistically significant difference to be identified.

The tested product has a good safety profile, both generally and as evaluated by liver analysis (AST and ALT). The presence in the product of two water-soluble and viscous fibers, psyllium and glucomannan, well known for their laxative properties (27, 28), could, in sensitive subjects, have caused some gut discomfort, this being the only side effect reported in one case.

Our preliminary results show that, in subjects poorly adherent to a hypocaloric diet and physical exercise regimen, a mixture of water-soluble, viscous fibers together with phytosterols/phytostanols could help tackle overweight/obesity, post-prandial hyperglycemia, and moderately raised levels of cholesterol and TG.

Our study has some limitations. Surely, it was too short (4 weeks) to really evaluate the effect of a lifestyle intervention which could need a double time, or more, to be correctly verified. In our opinion a very short trial like ours, analyzing the effects on subjects poorly adherent the lifestyle intervention, from an ethical perspective, was acceptable. Other limitations are: there were too few enrolled subjects, even if enough for the statistical analysis of the parameters considered; the study was not randomized or placebo controlled and, above all, it was not blinded. Anyway, our preliminary results suggest that this type of nutraceutical products could be used as add on therapy to lifestyle interventions especially for those patients known for not being totally adherent to life changes proposed by physician.

Disclosure

F. Di Pierro is the Scientific Director of Velleja Research, the company that developed the product tested in this study. A. Bertuccioli and G. Rapacioli are consultants with Pharmextracta.

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