

Evaluation of a Combined Approach to Weight Loss

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Abstract

Background: We are facing an epidemic of obesity. New approaches are required.

Aim of the study: To evaluate the weight-loss and fat-loss promoting effect of a novel dietary/activity program in conjunction with a nutritional supplement formulation.

Materials and methods: The design was prospective and randomized. 67 subjects met the inclusion criteria. Randomization produced three groups in the ratio 3:5:5 (Group 1:Group 2:Group 3). Group 1 received placebo and followed their usual diet and activity regimen. Group 2 received placebo and specific activity and dietary instructions. Group 3 received active product and the same diet and activity instruction as Group 2. Primary end points were weight and fat loss during the study.

Results: Group 2 lost statistically more weight and fat than Group 1. Group 3 lost statistically more fat and weight than did both other groups.

Conclusions: These results document the efficacy of a diet and activity program in producing meaningful weight loss. The nutritional supplement formulation significantly enhanced the amount of weight and fat loss and produced marked appetite suppression.

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INTRODUCTION

Obesity is one of the most pressing health issues in the United States. [1] An array of health conditions directly related to excess adiposity includes arthritis, stroke, heart attack, diabetes, hypertension, dyslipidemia, renal disease and even memory loss and dementia. [2,3,4,5,6,7,8,9,10] Last decade one in four Americans was obese. Now it is one in three. [11] We are eating too many calories for current activity levels. The nutritional content of our diet has fallen while the calorie content has increased. The consumption of an array of processed food products including trans fats, sugar and high-fructose corn syrup has risen and other factors (such as gluten in the diet) may play a role in the epidemic of nutritionally-based health problems. Most Americans are not receiving recommended amounts of the

most basic nutrients. These factors, and others, have conspired to place our health, and that of our country, in jeopardy.

Education, research and new approaches are urgently required. The purpose of the current human clinical trial is to examine an easy to follow diet and activity program in conjunction with a novel combination of nutritional supplements designed to enhance and facilitate weight loss.

MATERIALS AND METHODS

DESIGN

The trial was prospective, randomized, placebo-controlled and double blind in design. Participants were recruited by TV advertising from local physician practices. Each was required to satisfy the inclusionary and exclusionary criteria and pass compliance testing. The age range was from 22 to 67 years (mean 46) and included males and females who were overweight and wished to participate in a weight loss trial. The trial duration was six weeks after a one-week run-in period. Randomization produced three groups of subjects.

Group 1 was given placebo and was required to remain on their usual diet and activity program. Group 2 was given placebo and was provided instruction regarding diet and activity (similar in degree to Group 1). Group 3 was given active product and was advised to use the same diet and activity regimen that Group 2 followed. Each subject was required to sign an informed consent and was free to leave the trial at any time. The Liberty Investigational Review Board (Deland, Florida) reviewed and approved the consent form, study design and ethical considerations of the design protocol. All subjects were treated equally and confidentiality was assured. Each subject had been weight stable without any dietary changes prior to enrollment in the study. No subjects were taking any OTC products or pharmaceutical products known to affect weight. As determined by the physician overseeing the study, persons with severe comorbid diseases were excluded. These included active cancer, psychiatric disease, cognitive dysfunction, severe organ disease including liver, heart and kidney disease, untreated diabetes, or any females who were pregnant or were attempting to become pregnant. Excessive ethanol consumption was exclusionary.

Diet counseling was provided to Groups 2 and 3. Group 1 subjects were required to continue to eat their usual diet. All subjects did their own food shopping and food preparation. Recommendations for Groups 2 and 3 were to shop around the “periphery” of the grocery store. This is where fresh fruits and vegetables, fish, meat, dairy products and nuts and seeds are generally located. Non-starchy fruits were suggested. Subjects were told to avoid products containing trans-fats, processed foods and refined carbohydrates such as cookies, candy, soda and products containing sugar and HFCS (high-fructose corn syrup). It was suggested that they eat periodically throughout the day. No caloric restrictions were placed. Subjects were told to eat when they were hungry. Portion control was discussed. In addition, Groups 2 and 3 were given flax seed oil and were told to include it in their daily diet as a source of -linolenic acid, an essential omega-3 fatty acid. Food logs were kept and were reviewed during the one-week run-in period and every other week thereafter. Ongoing dietary counseling was provided. Compliance was monitored.

Group 1 subjects were required to participate in their customary activity program on a regular basis. Compliance was monitored regularly. Group 2 and 3 subjects were instructed in an activity program that consisted of aerobic activity (thirty minutes per session) three times per week

(usually walking), wore a pedometer and were asked to increase their distance walked about 10% each week. They were also required to participate in light resistance activity (using light weights) for twenty minutes twice per week. All subjects were evaluated for compliance to their recommended activity regimen. Non-compliance (meaning less than 80% of the daily suggested amount) was grounds for removal from the study.

All subjects were required to attend meetings for one week prior to enrollment in the study and for the duration of the six week clinical trial. At each meeting information was disseminated, dietary and activity discussions were included and support was provided to encourage the continued participation of the subjects. Each subject was paid \$125 for participation in the study.

Each participant took three capsules (one serving) of either placebo or active product three times per day just prior to meal times. The product and placebo were both manufactured in a GMP accredited facility in the United States. Each bottle was coded and the bottles, the capsules and the contents were designed to assure an identical appearance. Throughout the trial, subjects were evaluated for adverse reactions by administration of a questionnaire and questioning by the trial coordinator.

One serving of active product contained: Vitex agnus castus, aspartic acid, calcium pyruvate, biotin, L-carnitine, chromium polynicotinate, desiccated fish oil and Garcinia cambogia fruit extract (50% hydroxycitrate). One serving (three capsules) of placebo contained an equivalent weight of a combination of sodium caseinate and sodium lactate in appropriate amounts to match the macronutrient composition of the active product. The active product had been previously studied in a metabolic hood trial at a major university and was found to have thermogenic activity. (Private communication)

Weight and body fat content were determined (using the BodPod, Life Measurements Inc. (Concord, CA)) at baseline and every two weeks throughout the study. Blood pressure and heart rate were determined at baseline and every two weeks throughout the study. Compliance was tested every two weeks for diet, activity and consumption of pills (by counting the number of pills in the 2-week bottle supply that was brought in every other week). If more than 10% of the pills were remaining, the subject was removed from the study.

STATISTICAL ANALYSIS

After the one-week run-in period, 67 subjects were randomized into three groups. Group 1 contained 17, Group 2 contained 25 and Group 3 contained 25 subjects. There were 5 subjects who dropped out of the study or were removed for non-compliance.

Group means and SEMs (standard error of the mean) were computed for each of the study parameters and group differences were analyzed for statistical significance which was set at P<0.05. The SPSS (Chicago, IL) statistical package was used to perform the statistical analysis.

RESULTS

There were no statistically significant (P<0.05) differences regarding clinical or demographic factors between the subjects in any of the groups at baseline except as noted below. These included age, baseline weight, behavioral variables (such as smoking status, caffeine intake and ethanol ingestion) and health risk profiles. (See Table 1.) There were no changes in blood pressure or heart rate in any group during the study. (Not shown)

Figure 1

Table 1: Clinical and Demographic Baseline Information

Parameter	Group 1	Group 2	Group 3	P value
Number	17	25	25	
Age (Years)	44.1	46.0	48.2	0.35
Height (cm) +/- SEM	162.8 (7.0)	167.9 (9.8)	164.6 (10.8)	0.07
Weight (lbs) +/- SEM	195.6 (24.8)	224.5 (45.1)	199.7 (40.9)	P12<0.014*
BMI [†] +/- SEM	33.9 (5.3)	36.0 (5.5)	33.4 (5.6)	0.08
Education (y)	13.9	15.1	14.6	0.33
Energy	3.44	3.72	3.56	0.69
Sleep quality	2.19	2.36	2.60	0.43
Caffeine	1.65	1.94	2.02	0.37
Smoking	4	6	6	0.19
Alcohol (drinks per week) +/- SEM	1.6 (1.8)	1.2 (1.9)	1.4 (1.5)	0.55
Gender (% F)	100	72	88	0.08
Cancer	1	2	1	0.46
Arthritis	7	6	9	0.47
Neuro Disease	1	0	2	0.37
Anemia	1	2	0	0.39
Migraine	5	9	6	0.85
Skin Disease	4	3	3	0.51
Food allergy	4	3	6	0.50
Diabetes	1	3	3	0.78
Hypertension	5	10	5	0.30
Thyroid disease	3	6	3	0.54
Asthma	5	3	1	0.06
Heart Disease	0	1	1	0.70
Depression	4	12	6	0.13
Surgery	10	16	14	0.84
GERD	4	9	7	0.67
Lipid disorder	5	4	6	0.58

* P12 refers to the P value comparing the difference between Groups 1 and 2. The P values comparing Groups 1 and 3 and between 2 and 3 were NS.
[†] BMI refers to Body Mass Index

The average weight of subjects in Group 2 was statistically greater than those subjects in Group 1 (NS compared to Group 3). The BMI of Group 2 was not statistically different from either of the other 2 groups.

There were statistically significant differences between each of the groups regarding weight loss and fat loss. (See Tables 2 and 3) Group 3 lost significantly more weight and fat than those in Group 1 and 2. Group 2 lost significantly more weight and fat than those subjects in Group 1. Appetite suppression was significantly higher in Group 3 than Groups 1 and 2. (See Table 6) 100% of the subjects in Group 3 lost weight. (See Table 4) 40% of the subjects in Group 2 and 88% of the subjects in Group 3 lost more than 5 pounds in six weeks. (See Table 5)

Figure 2

Table 2: Weight Loss Data Over Six Weeks (pounds +/- SEM)

	Group 1	Group 2	Group 3
Weight Loss	0.04 +/- 3.2	4.40 +/- 4.4	11.77 +/- 5.5

P < 0.0001 (Group 1 vs Group 2)

P< 0.001 (Group 2 vs Group 3)

P< 0.0001 (Group 1 vs Group 3)

Figure 3

Table 3: Fat Loss Data Over Six Weeks (pounds +/- SEM)

	Group 1	Group 2	Group 3
Weight Loss	0.04 +/- 3.2	4.40 +/- 4.4	11.77 +/- 5.5

(Positive numbers mean weight loss; negative numbers mean weight gain)

P< 0.001 (Group 1 vs Group 2)

P< 0.001 (Group 2 vs Group 3)

P< 0.0001 (Group 1 vs Group 3)

Figure 4

Table 4: Percentage of Subjects That Lost Weight in Each Group (%)

Group 1	Group 2	Group 3
56	80	100

P= NS (Group 1 vs Group 2)

P< 0.05 (Group 2 vs Group 3)

P< 0.001 (Group 1 vs Group 3)

Figure 5

Table 5: Percentage of Subjects That Lost > 5 pounds of weight (%)

Group 1	Group 2	Group 3
6	40	88

P< 0.0001 (Group 1 vs Group 2)

P< 0.001 (Group 2 vs Group 3)

P< 0.0001 (Group 2 vs Group 3)

Figure 6

Table 6: Marked Appetite Suppression (%)

Group 1	Group 2	Group 3
0	25	80

P= NS (Group 1 vs Group 2)

P< 0.001 (Group 2 vs Group 3)

P< 0.0001 (Group 1 vs Group 3)

There were no significant adverse reactions in any group and minor reactions were not significantly different among the groups. They consisted of mild indigestion, loose stools and were transient. None required removal from the study.

DISCUSSION

The clinical trial documented a statistically significant weight and fat loss between Group 2 and Group 1, between Group 3 and Group 2 and between Group 3 and Group 1. This confirmed a beneficial effect on weight loss and fat loss by the recommended program of diet and activity. It also confirmed a substantial magnifying effect on weight loss by the unique combination of nutritional supplements.

A prior nutritional product containing some of the current components was previously examined in a similar fashion. [12] The proposed mechanism of action was discussed in detail in that article. The current nutritional formulation represents a significant evolution from the prior product but incorporates some of the basic metabolic physiology. Both nutrient formulations contain ingredient combinations believed to turn on futile carbohydrate metabolic cycles in the liver. [12] A futile metabolic cycle is a cyclical pathway that starts and ends with the same metabolic product (such as product A " B " C " D " A). When this pathway is covered at a metabolic cost (meaning energy in the form of ATP (adenosine tri-phosphate) is consumed), this defines an example of a thermogenic pathway. If such a pathway is covered repeatedly, many ATP molecules are consumed and, if repeated, may contribute to weight loss. In a separate human study, this nutrient supplement formulation was shown to enhance oxygen consumption and was found to have thermogenic properties. (Private communication)

The current formulation also includes extracts from the fruit of *Vitex agnus castus*. It has been demonstrated that specific components in *Vitex agnus castus* bind to and activate

dopamine D2 receptors in the brain. This effect augments central dopaminergic neurotransmission. [13,14]

It is well known that factors other than hunger are responsible for different aspects of eating behavior. Overeating has even been considered to be an addictive behavior with food as the desired source of pleasure. When other addictions are investigated including smoking, eating, excessive alcohol ingestion, sex and even video games, dopaminergic pathways in the brain have been demonstrated as playing a key role. [15]

It has been hypothesized that a significant number of persons who overeat do so because they are unable to satisfy their food craving due to an inability to engage dopaminergic neurons. [16] This then requires them to consume more food (to provide a larger stimulus) in order to satisfy their food cravings. This observation can be reflected in elevated dopamine neurotransmission. These individuals (who overeat for the reasons discussed above) appear to have a relative inability to activate central dopamine pathways and require a more potent stimulus (meaning higher food intake).

Clinical evidence for this behavior is supported by observations from diverse clinical settings including failure to thrive in children treated with amphetamines or other stimulant medications (that enhance dopamine neurotransmission) for ADD and ADHD. [17] Dopamine agonist therapy for other conditions such as Parkinson disease or disorders due to excessive prolactin release (such as prolactin secreting pituitary tumors or various perimenstrual syndromes) is also associated with appetite suppression. [18,19] One mechanism involves decreased dopamine reuptake in the synaptic cleft and the other a direct D2 receptor binding effect. Both approaches have similar results. *Vitex agnus castus* has been shown by competitive binding studies to bind to and activate central dopamine D2 receptors. [13,14] For this reason, it was included in the formulation for its potential impact on satiety.

The diet and activity arm of the program was felt to be unique. Numerous prior studies have supported a connection between exercise and weight loss. Exercise also has numerous physical, emotional and other well-documented health attributes. We recommended a program that was easy to follow and that the subjects enjoyed. It included both aerobic and resistance-training components that could be performed in a convenient fashion and were felt to be compatible with modern lifestyles. It did not require spending long periods in the gym but could be done at or

near home and with minimal cost or inconvenience.

There has been much written in the medical literature about different dietary approaches and their impact on weight and other health parameters. The primary suggestions recommended here were to eat when hungry, learn what the early signs of satiety were and to consume fish, flax oil and other fresh minimally or unprocessed foods. It was suggested that starchy foods be limited and that sugar, HFCS (high-fructose corn syrup) and trans fats be avoided. No recommendation was made to restrict calories.

One unique dietary recommendation in this study was the inclusion of flax seed oil. It is the richest source of the essential omega-3 fatty acid -linolenic acid. Modern diets are frequently deficient in omega-3 fatty acids. However, somewhat surprisingly, a large proportion of dietary -linolenic acid, rather than being elongated into DHA (docosahexanoic acid), is oxidized in the liver with the subsequent formation of ketone bodies. [20] Ketone bodies are able to be metabolized by neurons in the brain and are another nutrient substrate, in addition to glucose, that provides an energy source for nerve cells. This effect of ketone bodies (acting as an additional energy substrate for neurons) is believed to stabilize appetite as well and for this reason was included in the dietary protocol.

The complete program consisting of diet, activity and consumption of a unique combination of nutritional supplements was designed to enhance weight loss and fat loss. As shown in this clinical trial, it was effective at achieving both goals. Together, the nutritional supplement and the diet and activity program had a potent appetite suppressive effect. In addition, every subject in Group 3 lost weight (25/25).

CONCLUSION

The nutrient composition and the dietary and activity recommendations evaluated in the current study were well tolerated, easily complied with and produced significant losses of weight and fat throughout the trial.

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