Effect of the GOLO Diet and Release Supplement on Weight, Glycemic Control and Indicators of Insulin Sensitivity in Overweight and Obese Patients with Type 2 Diabetes

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Summary: 26 subjects with type 2 diabetes mellitus were recruited in an open-label study of the GOLO Diet with Release supplement at a single clinical site. 15 subjects completed the study over the 13-week treatment period. Overall weight loss averaged 7.9 lbs. (-3.8%) and BMI levels dropped by 1.3 (-3.7%). Markers of glycemic control improved with Hemoglobin A1C (-9.2%) and fasting blood glucose (-17.9%) decreasing while markers of insulin resistance including insulin levels (-18.7%) and HOMA-IR (-36.6%) showed substantial improvement. Favorable improvement was also noted in other laboratory results and clinical measures including cholesterol levels and inflammation.

Introduction: Excess body weight from overeating, poor nutrition and lack of exercise is highly correlated with health status. Clinical weight loss in overweight and obese people is associated with improvements in clinical markers of health, including key measures of blood sugar and blood lipids used to determine a person's health status.

Populations who are overweight and obese include people who exhibit a wide range of blood sugar levels, ranging from healthy to pre-diabetic to type 2 diabetes. Overweight and obese people on this spectrum often have difficulty obtaining meaningful or sustained weight loss. Body weight is also a leading indicator of high blood sugar levels. It is well established that people who are healthy, pre-diabetic or diabetic who lose weight and exercise tend to lower their measures of blood sugar and blood lipids, and are more likely to improve their health status (1).

GOLO has created a weight management program (GWMP) that includes a supplement known as Release and is designed to help people who are overweight or obese get the proper balance of macro and micro nutrients from conventional foods, eat the proper portion size and combinations to help keep insulin steady for weight loss, and help them to transition to a healthier lifestyle. The GWMP includes a point-based system from the four macronutrient food groups that is based on the individual's activity level and body mass. Additionally, the program includes common-sense instructions, motivation and tips supporting compliance and recommends a minimum of 15 minutes of exercise per day. The Release dietary supplement contains 7 plant-based ingredients and 3 minerals including zinc and chromium, essential nutrients that support regulation of blood sugar.

In case studies from clinician and wellness program use, GWMP has shown the ability to reduce body weight in both healthy and diabetic people who are overweight or obese. Secondary endpoints including measures of blood sugar have been observed to decrease because of the GWMP program (2).

While the GWMP has been developed and used in both healthy overweight and type 2 diabetic people, more systematic research is needed to determine to what extent it is able to support healthy weight loss. This open-label pilot study is intended to observe the effects of the program in a representative group of subjects with type 2 diabetes at one outpatient medical practice.

Study design: This observational study evaluating the effect of the GOLO Weight Management Program with Release supplement (GWMP) on weight and metabolic syndrome indicators in overweight or obese subjects with type 2 diabetes mellitus was conducted at one clinical site in the United States. The study consisted of 4 visits over approximately 13 weeks.

At visit 1, study eligibility was determined and subjects were given the commercially available GOLO Weight Management Program and instructed on the program's diet and exercise guidelines. Subjects were given the Release supplement and instructed to take one capsule three times a day with meals. Laboratory and body measurements were obtained. Visit 2 consisted of a telephone call to subjects to assess tolerability of the program. At approximately week 4, subjects returned for Visit 3 for a compliance and tolerability assessment and body measurements. The final visit 4 occurred at approximately week 13 and included body measurements, laboratory analysis and compliance and tolerability assessment.

Body measurements included fasting weight, height, waist and hip circumference, and resting blood pressure and pulse were taken at each visit. A Tanita scale was used to calculate BMI, body fat and visceral fat. Laboratory evaluation included hemoglobin A1C, fasting insulin, fasting blood glucose, lipid panel, metabolic panel including liver testing, hsCRP, CBC, sex hormones, and PSA in men. Homeostatic model assessment of insulin resistance HOMA-IR was calculated using the formula (Fasting Blood Glucose) (Fasting Insulin)/22.5(3). Stress and Anxiety were measured at visit 1 and visit 4 using a standardized Stress Questionnaire.

Subjects: 26 subjects consented to participate in the study. One subject screen failed for a BMI outside of inclusion criteria. 10 subjects withdrew or were removed from the study for the following reasons: 5 lost to follow-up/voluntarily withdrew, 3 adverse events and 2 poor study compliance. 15 subjects completed the study and attended all 4 visits.

Results: 5 Males and 10 Females completed the study. The average age of males was 57.8 and females 58.5. The average starting weight was 206.3 pounds and BMI 34.3 which is considered obese. Average hemoglobin A1c (7.5) and fasting blood glucose (153.7) were elevated at baseline indicating poorly controlled type 2 DM. Initial resting blood pressure (124.1/75.5) and LDL cholesterol (100.5) were already at or near goal levels in this group of diabetic subjects, primarily due to pre-study treatment with blood pressure and cholesterol medications.

Changes from baseline visit 1 to visit 4 in weight, BMI, body analysis and body measurements are listed in Table 1. Overall weight loss averaged 7.9 lbs. (-3.8%) and BMI levels dropped by 1.3 (-3.7%). Loss of Fat Mass (-7.2%) was more pronounced in this overweight/obese population. Waist measurements (-6.1%) improved more than hip measurements (-3.5%) resulting in a favorable change in waist/hip ratio (-6.1%). Changes in resting blood pressure and pulse were minimal as most subjects were pre-treated with blood pressure medication as is standard care in diabetic patients. Changes in the Stress/Anxiety survey were substantial (-49.0%).

Changes from baseline visit 1 to visit 4 in markers of glycemic control and insulin sensitivity are listed in Table 2. Levels of Hemoglobin A1C (-9.2%), a measurement of DM control over a 3-month period improved, while fasting blood glucose improvement was even more pronounced (-17.9%). Markers of insulin resistance, an important cause of type 2 DM and other diseases, decreased greatly with insulin levels falling (-18.7%). HOMA-IR, a standard calculation of insulin resistance, dropping even more extensively (-36.6%).

Changes from baseline visit 1 to visit 4 in total and LDL cholesterol levels were minimal but favorable in this group of subjects that generally were already being treated with statin medications. Improvements in HDL levels were more substantial (3.4%) as were improvements in triglyceride levels (-12.1%). Levels of hsCRP a marker of general inflammation and associated with cardiovascular risk were reduced (-2.8%).

Tables:

Table 1: Changes in Weight and Body Measurements

	Visit 1 (Week 1)	Visit 4 (Week 13)	Change
Weight (lbs.)	206.3	198.4	-7.9 (-3.8%)
BMI	34.3	33	-1.3 (-3.7%)
Fat Mass (lbs.)	77.7	72.1	-5.6 (-7.2%)
Visceral Fat Rating	13.8	12.8	-1.0 (-7.2%)
Waist (cm)	113.6	106.7	-6.9 (-6.1%)
Hips (cm)	115	111	-4.0 (-3.5%)
Waist/Hip Ratio	1.77	1.66	-0.1 (-6.1%)
Stress/Anxiety Score	10.5	5.3	-5.1 (-49.0%)

Table 2: Changes in Markers of Glycemic Control and Insulin Resistance

	Visit 1 (Week 1)	Visit 4 (Week 13)	Change
Hemoglobin A1C	7.5	6.8	-0.7 (-9.2%)
Insulin Level (uIU/ml)	15.8	12.8	-3.0 (-18.7%)
Fasting Glucose (mg/dl)	153.7	126.3	-27.5 (-17.9%)
HOMA-IR	6.5	4.1	-2.4 (-36.6%)

Table 3: Changes in Lipid Panel

	Visit 1 (Week 1)	Visit 4 (Week 13)	Change
Total Cholesterol (mg/dl)	179.1	177.2	-1.9 (-1.0%)
LDL Cholesterol (mg/dl)	100.5	99.8	-0.7 (-0.7%)
HDL Cholesterol (mg/dl)	43.7	45.2	1.5 (3.4%)
Triglycerides	183.1	161.0	-22.1 (-12.1%)
hsCRP	5.5	5.3	-0.2 (-2.8%)

Table 4: Changes in Liver Transaminases and Sex Hormones

	Visit 1 (Week 1)	Visit 4 (Week 13)	Change
AST (mg/dl)	28.2	24.7	-3.5 (-12.3%)
ALT (mg/dl)	34.4	29.9	-4.5 (-13.0%)
Progesterone (women)	1.1	.3	-0.8 (-76.9%)
Estradiol (women)	34.4	24.8	-9.6 (-27.9%)

Discussion: Among the 15 subjects completing this study, weight loss was demonstrated and averaged 7.9 pounds over 13 weeks. This weight loss is impressive because treatments for type 2 DM often are associated with weight gain (3). One explanation for the weight gain usually seen in diabetic patients is that as blood sugar control is improved with intervention, less glucose is generally lost through renal oversaturation (glycosuria), retaining these calories, and weight gain is often seen initially with diabetic treatments (3). Generally, any weight loss achieved in the first 3 months of diabetes treatment is considered important. In addition, the preferential loss of fat mass as demonstrated in this study is particularly desirable in treating type 2 DM.

Improvements in glycemic control and insulin resistance were the most impressive results of the study. Hemoglobin A1C and fasting blood glucose over 13 weeks compares favorably with traditional oral anti-diabetic treatments like metformin or pioglitazone (4). While the initial average A1C at baseline (7.5) indicated poor diabetic control, the average A1C level at V4 (6.8) met the goal A1C level recommended for diabetic patients (less than 7.0) (1). Changes in fasting insulin level and HOMA-IR actually exceeded that seen with these prescribed medications (4). The large improvements in insulin resistance demonstrated by the GWMP system with the Release supplement suggest a beneficial role in other disease states including the Metabolic Syndrome.

Favorable changes to other laboratory tests were observed from baseline visit 1 to visit 4 and are listed in Table 4. Improvement in liver transaminase enzymes (AST and ALT) are often seen with weight loss and most likely reflect decreased inflammation from fatty liver (5). Changes in sex hormones are also seen following weight loss and represent decrease peripheral fat conversion of hormone pre-cursers and suggest a benefit in patients with Polycystic Ovary Disease (PCOS) (6). No other significant changes in metabolic panel values, PSA or other safety variables were observed. Three subjects terminated from the study due to gastrointestinal adverse events including loose bowel movements or abdominal cramps. No serious adverse events were identified.

The Stress/Anxiety questionnaire was a 20-question self-administered written test that served as a general marker of psychological health. Although the study was not statistically powered for this endpoint, the change in average score on this questionnaire was impressive (-49%) and suggest the opportunity for further study.

The study was limited by selection of subjects at only one clinical site. In addition, the study was open-label and lacks the rigor of a double-blinded placebo-controlled study. In addition, poor subject compliance with the GWMP diet and exercise component may also have

influenced the results of the study. Although compliance with the Release supplement as obtained by pill counts (95 percent overall compliance by pill count) was excellent, compliance with diet and exercise recommendations was variable and more difficult to quantify. The relatively high drop-out rate (10/25- 40%) of the subjects consented for the study reflect this difficulty in obtaining compliance with the program. Frustration with previous diet plans and unrealistic expectations about lifestyle change likely contributed to drop outs. In addition, enrolling a population with type 2 diabetes that likely has failed other attempts at diet, exercise and medical therapy presented challenges to compliance.

In summary, the GOLO Weight Management Program with the Release supplement demonstrated weight loss and improvement in glycemic control comparable to standard prescription anti-diabetic medications in this small, single center study. Improvements in markers of insulin resistance were impressive and exceeded those seen by existing anti-diabetic medications including the Gold Standard for treatment of insulin resistance pioglitazone. Further studies will be needed to evaluate the role of the GOLO Weight Management Program with the Release supplement in diabetic and non-diabetic populations.

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