CASE STUDY: **Impact of GLP-1 Receptor Agonist and Digestive Enzyme Supplementation on Gut Microbiome and Metabolic Markers in Obesity Management**

ABSTRACT

This case study reviews the medication class glucagon-like peptide-1 (GLP-1) receptor agonists, specifically semaglutide, initially approved for the treatment of blood sugar dysregulation and now approved for weight loss. It examines the impacts of the administration of semaglutide in an obese female Caucasian patient seeking medical weight loss. The purpose was to investigate adverse effects associated with this controversial approach to weight loss and determine if the implementation of Transformation's Healthy Gut Program could serve as a supportive solution to those impacted by the potential side effects related to this medication. Over a 5-month period, significant changes in gut microbiome composition and metabolic markers were observed. The patient experienced substantial weight loss (26.7 lbs, 12.2% of initial body weight) as well as changes in several metabolic and gastrointestinal markers. This case highlights the importance of monitoring gut health and implementing targeted interventions to optimize GLP-1 therapy outcomes in obesity management.

INTRODUCTION

Obesity is a global health concern associated with increased risks of chronic diseases. While lifestyle modifications remain the cornerstone of obesity management, pharmacological interventions like GLP-1 receptor agonists have been a growing area of focus. Semaglutide first received FDA approval in December 2017 for treating type II diabetes mellitus and since receiving its FDA approval for obesity in June 2021 (Shu et al., 2022) has quickly been shown to be the most effective of the GLP-1 medications for obesity (Shi et al., 2022). It has been shown to have the ability to decrease food intake via actions affecting the hypothalamus and brainstem; to slow stomach emptying; to protect and even increase beta cell mass; to alter taste perception and food palatability, which helps reduce intake; and to help reduce inflammation (Malik et al., 2022; Muller et al., 2019; Zhao et al. 2021). However, as with all medications, the class of GLP-1 medications has potential adverse side effects. While delayed digestion and gastric emptying can elicit promising results for weight loss, its impact on gut microbiome, nutrient status, detox pathways, and other potential adverse effects warrant further investigation. GLP-1 can affect the stomach, intestines, gallbladder, exocrine pancreas, and liver. For example, GLP-1 can inhibit gastric acid secretion and slow gastric emptying, which can delay the absorption of nutrients in the small intestine. GLP-1 may also regulate the secretion of digestive enzymes and pancreatic mass. Patients may develop gastrointestinal adverse events, namely nausea, vomiting, diarrhea and/or constipation, dysbiosis, and gastroparesis. To minimize the severity and duration of these potential side effects, healthcare providers and patients must be aware of appropriate measures to follow and prevent these

side effects while undergoing treatment. The following case study will investigate semaglutide, the impact Transformation's Healthy Gut Program has on common side effects associated with GLP-1 receptor agonists, and the ability of enzyme and probiotic supplementation to help mitigate microbiome and metabolic pathway imbalances that can occur while on this drug.

CASE STUDY

In this present case study, we have a 61-year-old Caucasian female presented with a BMI of 34 (obesity class 1), hypertension, and no history of diabetes. Her initial weight was 218.7 lbs. The patient reported a history of postmenopausal symptoms, including some night sweats, mood changes, and sleep disturbances. She also mentioned snoring as a concern.

Medical History:

Hypertension (managed with Valsartan 160mg)
Hypothyroidism (managed with Synthroid® 50mcg)
Postmenopausal (using Premarin® 0.3mg)
No history of smoking
Mild alcohol consumption (1-3 drinks per week)
No consistent GI issues or events constituting gut dysregulation prior to the study

Lifestyle and Dietary Considerations:

Sleep: average 6 hours per night, not feeling rested upon awakening
Exercise: daily walking (couple miles a day), some gardening
Diet: following a low-carb diet with no dairy
Food sensitivities: dairy

Typical Diet:

Breakfast: Fast Food or just coffee
Lunch: Leftovers
Dinner: cooked meat, vegetable, sometimes carbohydrate
Snacks: sometimes crackers with cheese, apple, or nuts in the morning
Fluids: water, coffee, tea, occasional zero-calorie sodas, weekend alcohol consumption
Caffeine intake: 1 cup of coffee and 1 cup of tea daily

Psychosocial:

In a long-term partnership
Occupation: Property Manager (previously Oil and Gas office manager)
Reports moderate work-related stress (7/10) and health-related stress (8/10)
Uses meditation and prayer as relaxation techniques

Family History:

No significant family history of obesity, diabetes, or cardiovascular disease reported

Patient Goals and Readiness:

Primary health concerns: overweight, high blood pressure, low testosterone, mood issues, poor sleep, snoring, and postmenopausal symptoms

Last felt well: 8 years ago
Trigger for health changes: menopause and divorce
Health goals: lose weight, improve overall health, reduce snoring
Moderately willing to modify diet and lifestyle, take supplements, and engage in regular exercise
Highly supportive household for implementing health changes

Treatment Plan:

Transformation's Healthy Gut Program was selected to address the types of GI imbalances such as nausea, bloat, constipation, and dysbiosis that can occur when starting GLP-1 treatment by supporting digestion and nutrient acquisition, reducing inflammation and toxicity, and promoting timely elimination of waste and microbiome balance. Transformation's Healthy Gut Program includes digestive enzymes, a protease formula, and a probiotic supplement. It was chosen for this case study to support the GLP-1 agonist and mitigate GI side effects.

A digestive enzyme formula taken with meals helps ensure proper assimilation and bio-availability of all nutrients supporting cellular health and repair of the mucosal lining. Complete digestion also minimizes food intolerances and supports a healthy immune system.

A protease formula taken between meals promotes optimal blood flow and efficient detoxification as well as help manage inflammation, supporting the overall health of all systems of the body.

A probiotic supplement further supports digestion and a strong immune system while maintaining a healthy gut environment.

Protocol and Products Used:

1 capsule Digest with each meal. Transformation's Professional Protocol™ Digest is a comprehensive and therapeutic enzyme blend high in lipase, protease, and carbohydrases to ensure complete digestion of all foods.

1 capsule Protease at rise, midday, and bedtime (away from food). Transformation's Professional Protocol™ Protease is a comprehensive and therapeutic blend of acid / alkaline / neutral proteases and peptidases that targets complete protein digestion when taken with meals. Taken at bedtime or away from meals, Protease supplies a comprehensive and therapeutic blend of proteolytic enzymes for systemic benefits.

1 capsule PureZyme at rise, midday, and bedtime (away from food). Transformation's Genesis of Good Health® PureZyme is a gentle protease formula with calcium to serve as a buffer for those more sensitive to the effects of systemic enzyme therapy. Like the Protease formula, when taken at bedtime or away from meals PureZyme supplies protease enzyme support to promote healthy circulation, immunity, inflammatory control, and detoxification. The patient was switched to PureZyme due to trouble tolerating the more therapeutic Professional Protocol™ Protease blend.

1 capsule Probiotic at bedtime. Transformation's Professional Protocol™ Probiotic is a therapeutic formula with 6 strains of probiotics totaling over 5 billion cfu per capsule to support repopulation of a healthy microbiome. This formula was also chosen because it contains lactoferrin.

Expected Outcomes From Healthy Gut Protocol:

Improved/maintained gut microbiome composition

Improved digestive function

Improved metabolic / inflammatory markers

Reduction in side effects of medication (gas, bloat, constipation, nausea)

Methods:

The patient was monitored weekly to evaluate side effects, weight changes, and medication adjustments by the primary care provider prescribing the medication. Weekly calls were scheduled with Transformation's research team to monitor tolerance of supplements once implemented so adjustments could be made as needed.

The patient was instructed to continue any medications prescribed prior to the study. No dietary restrictions were given to allow the researchers to see how the program performed on its own. The patient was not taking any other supplements prior to our study, and usage of any other supplements through the course of the study was prohibited to prevent additional variables in the research findings.

Symptoms and adverse events/changes were measured through symptom questionnaires completed at weekly follow-ups with her primary care provider and Transformation’s researchers.

Baseline serum labs were provided prior to starting. Additional serum labs, while helpful, were not included for this particular study. The researchers were focused on evaluating shifts in microbiome composition, digestive function, and metabolic pathways, which drove the decision to use stool and organic acid testing instead.

The GI-MAP® microbiome analysis from Diagnostic Solutions Laboratory was used to provide a comprehensive look at overall gut health. By measuring pathogens in the gastrointestinal system, it is able to determine microbes that are causing chronic illness. It also analyzes digestion, nutrient absorption, inflammation, and immune function.

The OAP™ organic acids profile assessment from Diagnostic Solutions Laboratory was used to identify dysfunction in key metabolic pathways. Dysfunctional metabolic pathways can negatively impact mood, energy production, and overall health while also providing insight into nutrient insufficiency, diet composition, toxic exposures, and microbial metabolism.

Labs were collected at baseline, after two months of semaglutide injection, and after two months of semaglutide injections combined with Transformation’s Healthy Gut Program.

RESULTS

GI-MAP®	Baseline	Second	Final	Reference
Microbiome Analysis	12/6/2023	1/26/2024	5/22/2024	
Inflammatory Markers				
Secretory IgA	2720	1026	549	510 - 2010 ug/g
Eosinophil Activation Protein	2.64	0.63	0.86	< 2.34 ug/g
Calprotectin	<dl	0	106	< 173 ug/g
Intestinal Permeability				
Zonulin	n/a	91.9	66.1	< 175 ug/g
Digestive Function				
Elastase-1	269	142	735	> 200 ug/g
Streatocrit	6	11	<dl	< 15 %
Keystone Bacteria				
Bacteroidetes	1.29e12	7.01e11	5.24e11	8.6e11 - 3.3e12
Firmicutes	1.12e11	2.41e11	9.43e10	5.7e10 - 3.0e11
Firmicutes:Bacteroidetes Ratio	0.09	0.34	0.18	< 1.0
Opportunistic Bacteria				
Enterococcus spp.	2.64e7	9.40e8	8.01e8	1.9e5 - 2.0e8
Bacillus spp.	<dl	2.23e7	2.74e6	< 1.76e6
Streptococcus spp.	4.76e3	4.20e3	4.84e3	< 1.00e3
Enterococcus faecalis	<dl	2.55e4	<dl	< 1.00e4
Enterococcus faecium	<dl	1.42e6	1.05e5	< 1.00e4
Klebsiella pneumoniae	<dl	5.02e3	1.33e4	< 5.00e4
Pathogens				
Norovirus GI/II	<dl	<dl	6.60e2	< 1.00e10
Helicobacter pylori	<dl	2.41e2	3.61e2	< 1.00e7
Commensal Bacteria				
Akkermansia muciniphila	<dl	<dl	<dl	1.0e1 - 8.2e6

OAP™	Baseline	Second	Final	Reference
Organic Acids Profile	12/8/2023	1/30/2024	5/22/2024	
Glucose Metabolism				
Glucose	31.6	<dl	11.8	< 15.2 mg/dL
Glycolysis				
Pyruvic Acid	28.2	39.5	30.4	< 67.4 nmol/mg
Lactic Acid	792.1	1330.7	385.7	12.2 - 458.2 nmol/mg
D-Lactic Acid	>200.0	160.8	79.1	< 88.3 nmol/mg
Tryptophan Metabolism				
Xanthurenic Acid	12.2	<dl	8.1	0.6 - 10.2 nmol/mg
Kynurenic Acid	60.2	102.7	29.8	7.8 – 54.0 nmol/mg
Quinolinic Acid	152.4	97.3	98.1	29.4 - 178.5 nmol/mg
Krebs Cycle Intermediates				
Citric Acid	776.4	2165.8	2237.1	203.0 - 3208.6 nmol/mg
Isocitric Acid	518.0	525.9	1119.8	137.1 - 794.9 nmol/mg
Succinic Acid	35.5	9.4	59	12.3 - 260.4 nmol/mg
Metabolic Processing				
β-Hydroxybutyric Acid	15.7	39.4	17.8	3.2-116.4 nmol/mg
Toxic Impact				
Glucaric acid	14.6	12.7	65.7	< 31.5 nmol/mg
Orotic acid	6.1	5.6	12.9	1.2 - 13.1 nmol/mg
pH	5.6	6.5	5.5	5.5 - 7.7
Oxalic acid	163.1	189.8	204.2	144.9 - 1749.5 nmol/mg
Microbial Metabolites				
Hippuric Acid	874.4	650.0	1343.2	198.7 - 3104.6 nmol/mg

DISCUSSION

This case study demonstrates the complex interplay between semaglutide treatment, gut microbiome, and metabolic health in obesity management. The significant weight loss observed (~26 lbs, 12.2% of initial body weight) aligns with previous studies on semaglutide efficacy for weigh loss.

The changes in gut microbiome composition over the course of treatment, as evidenced by the GI-MAP® microbiome analysis, provide valuable insights:

Inflammation Markers: Immunoglobulin A (Secretory igA, or SIgA) is the primary immunoglobulin in the intestinal mucosa. It represents a "first line of defense" in response to antigens and pathogens in the GI and respiratory tracts. In addition to protecting against pathogens, SIgA plays a major role in helping to maintain balance in the microbiome and protecting against exposure to food-derived antigens. The initial elevation in SIgA (2720 ug/g) and Eosinophil Activation Protein (2.64 ug/g) indicated elevated immune response to antigens in the GI tract. These levels improved to WNL with semaglutide only and continued to improve with the enzyme and probiotic protocol. Eosinophils are white blood cells normally present in the gut that support immunity and maintain the protective mucosal barrier of the gut lining. The Eosinophil Activation Protein (EDN/EPX) is secreted by eosinophils in response to infections (particularly viral infections), allergic reactions, and inflammatory responses. This value was elevated at baseline but WNL after taking semaglutide and the Healthy Gut Protocol. This change supports a possible reduction in inflammatory responses and improvement in GI lining. Calprotectin levels were within the normal range on all three check points. The rise in the final stool sample was most likely due to the pathogen encountered later in the study, not due to the implementation of the Healthy Gut Program or semaglutide. These findings suggest an overall reduction in inflammatory processes, which is consistent with the metabolic improvements observed.

Intestinal Permeability: Zonulin is a protein that opens intercellular tight junctions in the gut lining. Zonulin increases intestinal permeability in the jejunum and ileum and is considered a biomarker for barrier permeability. The baseline stool test did not include zonulin levels, however midpoint results showed elevated zonulin. This was expected due to low fiber in the diet and the impacts on digestive function associated with semaglutide use. Zonulin levels trended to a healthy range as the Healthy Gut Program was implemented suggesting, the protocol could be helpful for maintained gut barrier integrity while taking GLP-1 agonists. This is a positive finding, especially in the context of weight loss and changes in the gut microbiome.

Digestive Function: Elastase-1 is a digestive enzyme secreted exclusively by the pancreas, giving a direct indication of pancreatic function. Elastase-1 is unaffected by pancreatic enzyme replacement therapy. Elastase-1 levels initially decreased (269 to 142 ug/g) but then significantly improved (735 ug/g) by the final test, suggesting an initial decline in pancreatic enzyme production followed by a substantial improvement. This pattern may reflect an adaptation period to the semaglutide treatment, followed by enhanced digestive function, possibly supported by the enzyme supplementation provided with Transformation's Healthy Gut Program. Steatocrit measures digestion of fats. Fecal fats are normally emulsified by bile salts and absorbed in the small intestines. High levels of fat in the stool may be an indication of maldigestion, malabsorption, or steatorrhea. Both baseline and midpoint labs showed impaired fat digestion. This marker improved with the implementation of the Healthy Gut Program, further validating the benefit of and need for digestive support while on medications like semaglutide.

Keystone Bacteria: Gram-negative Bacteroidetes and gram-positive Firmicutes are bacterial phyla that dominate the entire human digestive tract, including the mouth, nose, throat, and colon. An abnormal result in one or both of these phylum suggests imbalanced normal microbes in the GI tract. Further, high Firmicutes and low Bacteroidetes (resulting in a high F/B ratio) suggest microbial imbalance which may be related to increased caloric extraction (from food), fat deposition, lipogenesis, impaired insulin sensitivity, and increased inflammation. High levels of Bacteroidetes in the gut are generally associated with a healthy gut microbiome and favorable metabolic outcomes. Conversely, a lower abundance of Bacteroidetes has been observed in obese individuals compared to lean individuals. Bacteroidetes levels decreased from the initial to the final test (from 1.29e12 to 5.24e11 org/g) while Firmicutes remained relatively stable. This result led to a slight increase in the Firmicutes:Bacteroidetes ratio (0.09 to 0.18), although it remained within the normal range. These changes may reflect alterations in diet and metabolism associated with weight loss and impaired digestion and fermentation associated with GLP-1 side effects. Altered pH can influence Bacteroidetes and impaired digestion can cause them to go down with excessive fermentation. We know diet is strongly associated with the gut microbiome composition, with fiber being a major player. A high-protein, low-carbohydrate diet, like the one the subject of this case was following, can decrease Bacteroidetes in obese people. High fiber and lactobaccilus are two ways to improve Bacteroidetes ratios, and we believe the introduction of a probiotic formula weighted heavily in these strains along with digestive support from the Healthy Gut protocol helped to improve the drastic shift seen upon administration of a GLP-1 agonist.

Opportunistic Bacteria: Many bacteria measured on the GI-MAP® are considered opportunistic pathogens, as they only cause disease and illness in some individuals, particularly the immune-compromised. Many individuals come into contact with opportunistic bacteria and experience no symptoms. Most sources consider these microbes to be normal in the stool. However, they can cause gastroenteritis and inflammation at high levels in vulnerable patients. Symptoms may include diarrhea, loose stools, abdominal pain, or even constipation. Overgrowth and excessive colonization by opportunistic bacteria may occur when the commensal bacteria are impaired by poor diet, antibiotic use, parasitic infection, or a weakened immune system. When intestinal permeability is present (see zonulin), these microbes could escape the lumen of the gut and infect extraintestinal sites. There was an increase in potentially opportunistic bacteria, including Enterococcus spp., Bacillus spp., Streptococcus spp., Enterococcus faecalis, and Enterococcus faecium. This shift might be related to changes in the gut environment due to digestive dysfunction while on semaglutide treatment and/or dietary changes that occur while on the drug. Many of these bacteria feed on undigested protein. Practitioners are encouraged to push protein while on GLP-1 drugs without considering the digestive changes that follow implementation of this medication. Ignoring digestive function, while pushing high protein, can cause more harm than good as evidence by the significant changes we see in opportunistic microbes.

H Pylori: H. Pylori was present in 2nd and 3rd stool findings. H. pylori bacteria are passed from person to person through direct contact with saliva, vomit or stool and most likely not related to GLP-1 or implementation of the Healthy Gut Program. This pathogen was most likely introduced during the subject's brief hospital stay for an unexpected foot surgery prior to the 2nd stool test. The researchers were not focused on H Pylori eradication, so no protocol adjustments were put in place to bring that number down. Had the researchers not been evaluating a specific protocol, we could have increased the amount of proteolytic enzyme to support bring H Pylori back to a healthy range as evidence from other case studies we have done using higher dosing of protease.

The rise in opportunistic bacteria could be due to H Pylori suppressing stomach acid allowing bacteria to grow. This could also be a side effect of the GLP-1 medication's gastric stagnation which gives opportunistic bacteria more food to eat. A positive finding here was many of these bacteria started to trend downward once digestive and probiotic support was provided with Transformation's Healthy Gut Program. The rise in Strep after implementing enzymes was not surprising. Protease is a biofilm disruptor, and Strep is a biofilm-forming bacteria. The increase in this level after introduction of the Healthy Gut protocol could be due to protease starting to peel back the layers of this particular biofilm. The persistence of these elevated levels suggests a need for ongoing monitoring and potential intervention to maintain a balanced microbiome. Klebsiella was another opportunistic organism that was elevated after GLP-1 medication had started. This bacterium could be related to the diarrhea she experienced, and it is also a bad histamine producer. Klebsiella can be very problematic so there is a need to get this level down. Supporting digestion, motility, and microbiome overcrowding may be effective at eradicating this bacteria based on findings in the final stool sample.

Pathogens: The appearance of low levels of Norovirus GI/II (6.60e2 org/g) and Helicobacter pylori (3.61e2 org/g) in the final test, while within reference ranges, warrants monitoring. Norovirus is a highly contagious virus that causes gastroenteritis, or inflammation of the stomach and intestines. This explains the rise in Calprotectin seen on the final stool draw, which we believe otherwise would have been WNL due to the anti-inflammatory and immunomodulatory properties seen with supplementation of proteolytic enzymes. These findings underscore the importance of ongoing digestive support and monitoring during weight loss interventions using GLP-1 agonist.

Commensal Bacteria: Consistently low levels of Akkermansia muciniphila (<1.00e2 org/g) throughout the study period suggest a potential area for intervention, as this bacterium is associated with metabolic health and gut barrier function. This keystone species and primary mucus degrader relies on fiber for food in order to generate mucus-derived sugars and metabolic products that support the growth and energy needs of other beneficial gut microbes. This bacterium is also an important factor in mucosal health and mucus production. Low fiber, high fat, high protein diets can starve this bacteria, resulting in it feeding on the mucosal layer for survival and resulting in intestinal permeability. Low levels are also associated with obesity and metabolic dysfunction. The persistence of low levels despite weight loss and metabolic improvements is noteworthy and may indicate a need for targeted digestive probiotic supplementation and additional prebiotics to protect intestinal barrier function.

The metabolic marker changes, as evidenced by the OAP™ Organic Acids Profile assessment, show significant improvements for the following:

Glucose Metabolism: nitial elevated Glucose levels (31.6 mg/dL) normalized by the end of the study (11.8 mg/dL), indicating improved glucose regulation, likely due to the combined impacts of semaglutide, digestive function, nutrient uptake, and weight loss.

Glycolysis: The Lactic Acid and D-Lactic Acid markers showed an interesting pattern. Initially elevated, they further increased in the second test, possibly due to changes in gut microbiota or metabolic adaptations. However, by the final test, both had normalized, suggesting an overall improvement in metabolism and potentially gut health.

Tryptophan Metabolism: The initial elevation in Xanthurenic Acid (indicating potential B6 deficiency) and Kynurenic Acid normalized by the end of the study. This could reflect improved B-vitamin status or altered tryptophan metabolism, possibly influenced by changes in the gut microbiome and improved digestion.

Krebs Cycle Intermediates: Citric Acid and Isocitric Acid levels increased over time, with Isocitric Acid becoming elevated in the final test. This change is more than likely related to dietary changes but could indicate changes in energy metabolism, possibly related to weight loss and altered gut microbiome.

Toxic Impacts: Toxic impact scores were more prevalent on final OAP™ draw, which points to a possible higher efficiency of toxic excretion from the enzymes and probiotics consumed. Further studies are needed to test this hypothesis and will be the goal of a larger scale study.

The patient experienced initial adverse effects from both the semaglutide injections and the enzyme supplementation:

Initial low energy and queasy stomach after the first semaglutide injection.

Ongoing need to be careful with food choices to avoid heartburn, which can occur as a side effect of the medication. Subject did experience relief from heartburn once enzyme protocol started.

Initial diarrhea, some heart burn and nausea with protease enzyme supplementation. This was resolved after protocol adjustment with a gentler protease blend. (Purezyme).

Temporary interruption in treatment due to foot surgery.

The low energy and queasy stomach reported after the first injection are common side effects of GLP-1 receptor agonists and typically improve over time. The ongoing need to be careful with food choices to avoid heartburn suggests a persistent, though manageable, side effect of semaglutide treatment with enzyme support. The patient's symptom questionnaire showed improvement with regards to heartburn and bloating with the enzyme protocol.

The subsequent adverse reactions to enzyme supplementation (diarrhea and heartburn) highlight the importance of personalized dosing and careful implementation of adjunct therapies. The successful resolution of these issues through protocol adjustment demonstrates the potential Transformation's Healthy Gut Program has for managing adverse effects without compromising treatment efficacy.

As the patient reported on March 28, 2024:

"Starting weight 218.7 now 198. Start date December 15, 2023. Now on .2 ml or .6mg. Shot 1 times a week. You have to be very careful what you eat so you do not have heartburn and sometimes I have heartburn anyway. I was doing very well but ended up with a cyst on the bottom of my foot that had to be operated on and removed. I did only miss 1 shot of semaglutide. I received anesthesia, a block knee down and a local in the bottom of my foot.

"My eating has gone well 2 meals a day. Protein, veggie, small carb. Meals are 1/2 or less of what I ate before. It does seem harder to drink the water I need each day, but I do concentrate on meeting my goal. My exercise has been stopped with not being able to walk well.

"I chose to do this study because I have always been interested in natural vitamins and I felt if I could get extra help with balancing my system maintaining the weight loss would be obtainable. I really like the Probiotic and Digest, I do not like Protease. Maybe it is because I work at balancing the way my stomach feels from the semaglutide anyway without a supplement that makes my stomach upset."

These experiences emphasize the importance of close patient monitoring and the need for a flexible, personalized approach when combining GLP-1 receptor agonist therapy with enzyme and probiotic supplementation. The ability to overcome these initial challenges while still achieving significant weight loss

and metabolic improvements speaks to the potential of this combined approach, but also highlights the need for careful management of side effects to ensure patient comfort and compliance.

The unexpected complication of foot surgery during the study period provides insight into the resilience of the treatment protocol. Despite a brief interruption in semaglutide administration and a pause in physical activity, the patient continued to lose weight and maintain improvements in metabolic markers.

CONCLUSION

This case study provides valuable insights into the effects of combined semaglutide, enzyme, and probiotic therapy on gut health and metabolic markers in obesity management. The patient achieved significant weight loss and improvements in several metabolic parameters despite facing challenges such as foot surgery and initial difficulties with semaglutide and enzyme supplementation.

We propose that adding probiotics and digestive enzymes alongside GLP-1 treatment could restore helpful gut flora, thereby improving gut function, reducing potential AE's, and reducing post-medication discontinuation weight regain from nutritional deficiency and dysbiosis. These findings highlight the potential benefits of monitoring gut microbiome composition and metabolic parameters during GLP-1 therapy as well as the importance of personalized supplement protocols. The normalization of several key metabolic markers and the improvement in digestive function by the end of the study suggest that this combined approach may offer comprehensive benefits beyond weight loss alone.

Future research should focus on larger-scale studies to validate these observations and develop evidence-based protocols for integrating gut health interventions into obesity treatment strategies. Particular attention should be paid to strategies for promoting proper digestion and microbiome seeding for beneficial bacteria while managing the growth of opportunistic organisms to mitigate side effects. Additionally, longer-term follow-up would be beneficial to assess the durability of these metabolic improvements, weight loss outcomes, and the long-term impact on gut microbiome composition.

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APPENDIX

Treatment Plan and Timeline:

December 1, 2023: Initial paperwork completed by patient. Informed consent was obtained from the patient for participation in the study and publication of this case report.
December 8, 2023: Baseline testing (stool/urine samples, Seca bioimpedance test, weight, BMI, microbiome analysis, organic acids test, and comprehensive blood panel).
December 15, 2023: First in-person appointment. Starting weight 218.7 lbs. First semaglutide injection administered.
December 18, 2023: Patient reports low energy and queasy stomach after first injection.
December 21, 2023: Patient reports 5 lbs weight loss after first week.
January 25, 2024: Stool sample collected for second round of testing.
January 30, 2024: Urine sample collected for second round of testing.
February 9, 2024: Weight 205.7 lbs, BP 117/78. Denies any issues with semiglutide. Dose increased to 0.75 mg twice a week.
February 16, 2024: Enzyme supplementation protocol initiated: Digest (1 capsule with meals), Probiotic (1 capsule at night), and Protease (3 capsules per day between meals).
March 1, 2024: Patient reports diarrhea and heartburn from supplements. Protocol paused.
March 5, 2024: Patient reports symptoms stopped after discontinuing supplements.
March 11, 2024: Patient missed one semaglutide injection due to upcoming surgery.
March 14, 2024: Foot surgery performed to remove a cyst. We were unable to confirm if IV antibiotics were given for surgery. Subject declined receiving antibiotic prescription post-surgery.
March 18, 2024: Semaglutide injections resumed. New dose: 0.6 mg twice a week.
March 28, 2024: Weight 198 lbs, BP 117/83. Modified supplement protocol: 1 capsule Probiotic and 1 capsule Digest with each meal, 1 capsule Protease at night. Tolerating increased dose of semiglutide well.
April 2, 2024: Stitches removed from foot surgery.
April 12, 2024: tolerating dose of semiglutide well. Wt 197 lbs, BP 118/72. Dose same .3 mg bi weekly. Released to return to exercising.
May 8, 2024: Weight 193 lbs, BP 124/84. Dose increased to .6 mg bi weekly.
May 13, 2024: Supplement protocol adjusted: 1 capsule Digest with each meal, 1 capsule PureZyme 2-3 times a day 30 min away from food (maintained 1-2), 1 capsule Probiotic at bedtime.
May 21-22, 2024: Final round of stool and urine tests conducted.
May 2024: Final blood work completed.
Total weight loss 25.7 lbs