ORIGINAL RESEARCH

The Use of Personalized Functional Medicine in the Management of Type 2 Diabetes: A Single-Center Retrospective Interventional Pre-Post Study

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ABSTRACT

Background • There is a subgroup of patients with type 2 diabetes (T2D) in whom traditional treatment does not work well. Traditional management of T2D does not address the autoimmune component seen in a subgroup of patients with T2D.

Primary Study Objective • We sought to evaluate the effectiveness of using a personalized functional medicine (PFM) approach to managing T2D.

Methods/Design • Patient files from 2010 to 2015 were culled for patients previously diagnosed with T2D and their deidentified data regarding medications and T2D biomarker test results were compiled. A total of 35 patients were contacted for permission to use their deidentified data for the purposes of this article. Of 35 patients, 11 provided written consent.

Setting • All participants had entered a single, private, integrative medicine clinic based in Maryland, USA.

Participants • The patient group consisted of 5 women and 6 men; age 50 to 77 years. Each patient was taking an antidiabetic medication and had reached a plateau in recovery, or wanted to reduce their medication intake. Allopathic physicians were retained by patients undergoing PFM treatment.

Intervention • After a thorough intake history was completed, necessary specimens were collected for analysis. Once test results were reviewed to identify nutrient deficiencies, intestinal dysbiosis, hormone imbalances, chemical burden and food immune reactivities, a personalized plan was developed for each individual patient. Each patient was retested appropriately during treatment. Treatment lasted from 2 to 10 months based on the patients' goals.

Primary Outcome Measures • The effectiveness of the PFM approach was measured by the reduction in medication needed to manage T2D and improvement in T2D biomarkers.

Results • At the end of PFM treatment, 6 patients were completely off T2D-related medications, and 5 had their doses reduced by 50%. Diabetes biomarkers improved: glucose decreased by an average of 78.36 mg/dL and hemoglobin A1c (HbA_{1c}) was lowered by an average of 2.71%.

Conclusion. In individuals not well-managed using traditional protocols, the PFM approach should be considered as an adjunct therapy. (*Altern Ther Health Med.* [E-pub ahead of print.])

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INTRODUCTION

The rate of type 2 diabetes (T2D) continues to rise worldwide. The Institute of Health Metrics calculated that in 2017 the global prevalence of T2D was 6059 cases per 100 000 population and projected an increase to 7079 individuals per 100 000 population by 2030.[1] The socio-economic burden of diabetes, and its associated disorders, includes rising insurance premiums, out-of-pocket expenses, lost work days, emotional stress and an overall lowering of the quality of life (QoL). The lifetime cost of managing T2D and associated disorders is estimated to be between $54 700 and $130 800, depending on the gender and age at which the person is diagnosed.[2]

Managing T2D traditionally involves the use of metformin and a sulfonylurea, along with diet and exercise counseling. This treatment has worked for many people with T2D. However, there is a subgroup of individuals with T2D who continue to struggle even when adhering to the treatment plan. This subgroup may be part of the 50% of patients with

T2D who have the same autoantibodies seen in type 1 diabetes (T1D), as reviewed by Itariu and Stulnig in 2014.[3] In these individuals, T2D is more complex than a metabolic disorder, in which the consequences of T2D are due to an interplay between genes and the environment.

The purpose of this study is to show the effectiveness of a personalized functional medicine (PFM) approach to treating individuals with T2D who have not been well-managed using solely traditional allopathic treatment methods.

STUDY DESIGN AND METHODS

Data Collection

Patient files from 2010 to 2015 were culled for patients previously diagnosed with T2D. Patients who sought treatment for better management of T2D were included in the review. Each patient's pertinent, deidentified data was collected on a single spreadsheet. The patients were contacted from July to August 2021, and of the 35 patients, 11 provided permission to use their deidentified information for the purposes of this publication.

Study Population

Patients previously diagnosed with T2D entered a single PFM clinic in the United States. Each patient had a prescribed allopathic treatment, was using an antidiabetic medication and had reached a plateau in their recovery or wanted to reduce the need for daily medication. Patients retained their allopathic physicians while undergoing PFM treatment, and during the PFM treatment, the patient's allopathic physician was the one who made changes to medication dosages.

Clinical Analysis

Before their first appointment, each patient completed a thorough PFM clinical history form. Blood, saliva, urine and/or stool samples were collected from each patient as necessary for evaluation. Patients were assessed individually with relevant laboratory testing to establish baseline levels and detect possible environmental triggers and/or immune dysfunction. In addition to traditional diabetes-related biomarkers, overall study testing included comprehensive blood chemistry, hormones, complete food immune reactivity, chemical body burden, pathogen burden, urinary organic compounds, nutrient deficiency and gut microbiome analysis.

Treatment

Test results from each patient were analyzed. The goals of each patient were taken together with the test results and a personalized treatment plan was generated. Patients were educated on which environmental triggers were exacerbating the diabetes, how to avoid them and how to implement lifestyle changes for a better quality of life (QoL) with diabetes.

Diet and Nutrient Deficiencies

Considering test results, health history and medication list, a nutritionist prescribed a food plan for each patient. The plan eliminated diabetes-triggering foods and common inflammatory foods, while increasing the intake of nutrient-dense foods. Each patient was educated using Dr Steph's Plate Rule© to ensure adequate intake of calories, proteins, fats and micronutrients. Recipes, food alternatives and meal plans were supplied to assist the patient with dietary changes. In some patients, food logs were requested to ensure compliance and for nutrient intake evaluation. Cronometer software was used to calculate and estimate nutrient intake and compare it with the patient's daily needs. Follow-up functional blood work was done 2 months after the patient began the program, and then every 3 months or as needed to evaluate for nutrient deficiencies. Alterations in dietary intake, frequency and variety were adjusted as treatment progressed. In some individuals, appropriate foods were reintroduced slowly, forms of fasting were advised, and macronutrient intake was modified to achieve desired results or to break through plateaus.

Chemicals

Some medications, poor nutrient intake, pesticide exposure, secondhand smoke and other chemical burdens can lead to impaired hepatic biotransformation. Some patients arrived with subclinical to clinical fatty liver disease, as well as varying levels of hepatic stress. Impaired liver detoxification may present as multiple chemical sensitivities, histamine reactions, constipation, headaches, skin rashes, imbalanced hormones and elevated liver hormones. Each patient's test results were evaluated, along with medical history. To avoid additional chemical exposures, patients were advised to eat food from organic, grass-fed and wild-caught sources. In addition, sauna usage, exercise and nutritional support of phase 1 and phase 2 liver detoxification pathways was provided, if necessary. Retesting occurred 8 weeks post protocols. If mold toxicity was identified, the Shoemaker Protocol[4] was used for treatment.

Pathogens

Pathogens can increase circulating glucose levels. Patients shown to be harboring pathogens were given treatment to boost their immune systems, make their bodies a less hospitable host for pathogens and eliminate them. Treatment included over-the-counter antimicrobials or medications prescribed by nurse practitioners or physician assistants as needed. Follow-up testing was performed after treatment to evaluate the effectiveness of the protocol(s).

Balancing the Microbiome

A healthy gut is essential for treating diabetes. Travel, medication, stress, diet, alcohol intake, hormone fluctuations and antibiotic use are some of the factors that influence the gut microbiome. When we identified a gut microbiome imbalance, antimicrobials were used for 8 to 12 weeks and retesting was performed. After retesting, maintenance treatment was advised, if necessary. Repeat testing was performed until a balanced intestinal microbiome was maintained.

Table 1. Diabetes-Related Medications Pre- and Post-Personalized Functional Medicine Treatment

Patient	Drug Class	Pre-Dosage	Reduced in (months, days)	Post-Dosage	Dosage Reduction
1	Metformin	2000 mg/day	10 m, 9 d	1000 mg/day	-50%
	Sulfonylurea	10 mg/day	10 m, 9 d	5 mg/day	-50%
2	ARB	25 mg/day	1 m, 25 d	0	-100%
	Sulfonylurea	5 mg/day	5 m, 5 d	0	-100%
3	Long-acting Insulin	40 units am 25 units pm	5 m, 1 d	0	-100%
4	Metformin	2000 mg/day	6 m, 27 d	0	-100%
	Sulfonylurea	10 mg/day	7 m, 17 d	5 mg/day	-50%
			1 m, 1 d	0	-100%
5	DPP4 inhibitor	100 mg/day	2 m, 13 d	0	-100%
	Sulfonylurea	5 mg/day	1m, 0 d	1.25 mg/day	-75%
			7 m, 5 d	0	-100%
	ACE inhibitor	10 mg/day	2 m, 13 d	5 mg/day	-50%
	Beta-blocker	100 mg/day	2 m, 13 d	0	-100%
6	Sulfonylurea	8 mg/day	3 m, 12 d	0 mg/day	-100%
7	Sulfonylurea	4 mg/day	0 m, 16 d	0	-100%
8	Metformin	1000 mg/day	5 m, 17 d	500 mg/day	-50%
9	Statin	40 mg/day	2 m, 2 d	20 mg/day	-50%
10	Long-acting Insulin	15 units/day	0 m, 15 d	0	-100%
11	Metformin	2000 mg/ day	4 m, 22 d	1000 mg/day	-50%
	Sulfonylurea	8 mg/ day	1 m, 26 d	4 mg/day	-50%
	DPP4 inhibitor	100 mg/ day	1 m, 26 d	0	-100%

Note: Patients 2, 3, 4, 6, 7, 10 no longer required diabetes-related medication. Patients 1, 8, 9 were able to reduce dosage by 50%. Patient 5 was allowed to stop 3 medicines, while the dosage of the fourth was reduced by 50%. Patient 11 no longer needed the DPP4 inhibitor, and the remaining 2 medication dosages were reduced by 50%.

Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blockers; DPP4, Dipeptidyl Peptidase 4.

Stress reduction and Improved Sleep

Elevated cortisol, working the night shift, poorly maintained sleep habits and high stress environments can trigger elevated glucose readings and exacerbate dietary intake complications (ie, late night eating). Patients with high stress were advised to make lifestyle and schedule changes and were prescribed sleep support and stress support supplements throughout the program. These patients were coached on sleep hygiene including reducing screen time, increasing physical activity and getting adequate sun exposure.

RESULTS

In this study, the patients, 5 women and 6 men, age 50 to 77 years, were clients of the PFM clinic for an average of 7 months (range 2 to 10 months). The most important marker was that each patient's allopathic physician reduced their medication within the time frame (Table 1). Of the patients, 6 came completely off all diabetes-related medication, while 5 were able to reduce or eliminate their medications.

Furthermore, each patient lost weight (2.27 to 16.33 kg), realized a decrease in body mass index (0.9 to 5.5 kg/m^2), realized an improvement in diabetes markers with glucose decreasing an average of 78.36 mg/dL and hemoglobin A_{1c} (HbA_{1c}) lower by an average of 2.71% (Figure 1).

It takes between 3 and 6 months to show marked improvement in cholesterol markers. Given the time frame, slight improvements were seen in the markers (Figure 2). The 2 patients with elevated total cholesterol (above 200), both brought their levels down to within a healthy range. A total of 6 patients had unhealthy levels of low-density lipoprotein (LDL), and all 6 were in healthy range at post-testing. High-density lipoprotein (HDL) readings were unremarkable. Of the patients, 5 had elevated triglycerides (TGs). All patients reduced their TGs; however, only 2 lowered them to a healthy range during the time of care.

DISCUSSION

We have presented cases showing the effect of adding PFM as a second-line approach to better manage T2D in patients in whom traditional treatment is not performing well. Our PFM model addresses not only the metabolic disorder, but also the associated immune dysfunction, hormone fluctuations, gut dysbiosis and environmental triggers that may be exacerbating the T2D. By eliminating the environmental exacerbators, regulating immune

Figure 1. Diabetes biomarkers pre- and post-PFM protocol. During the treatment period, a trend of improvement in glucose and hemoglobin markers was seen in all patients.

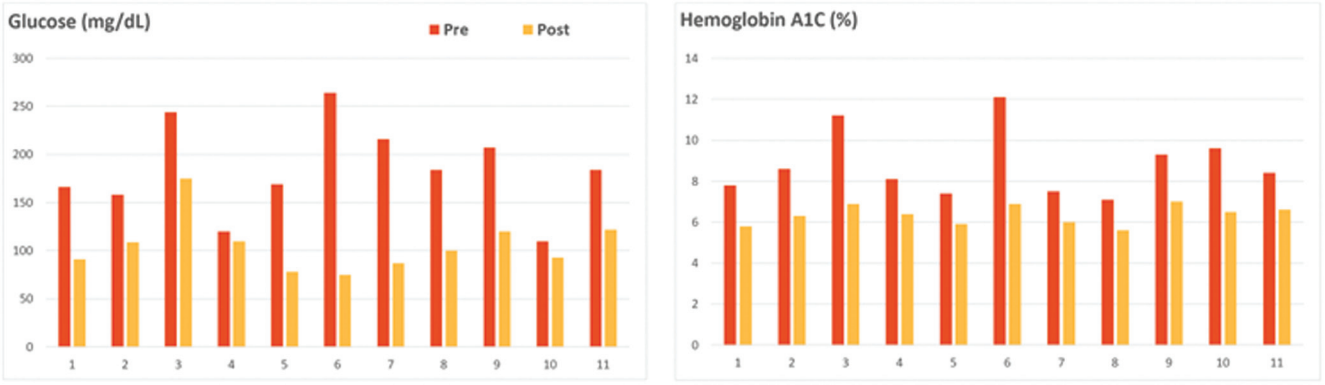
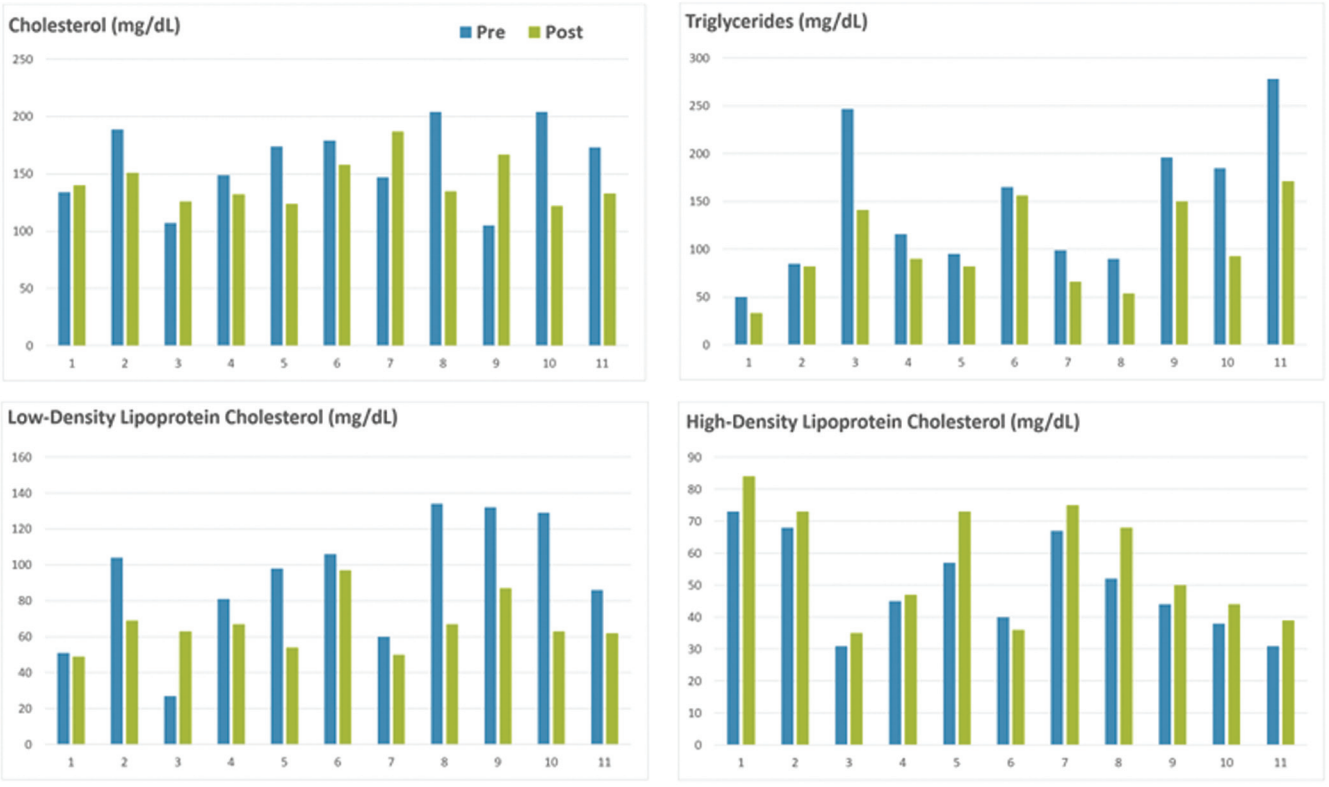


Figure 2. Cholesterol-related biomarkers pre- and post-PFM protocol. During the treatment period, a trend of short-term improvement was seen in cholesterol, tryglycerides, low-density lipoprotein and high-density lipoprotein; it is important to note that cholesterol-related biomarkers usually take longer to show improvement on test results.



functions and healing the gastrointestinal system, patients with T2D may have an improved QoL.

Detailed in the following paragraphs, environmental exacerbators include dietary proteins,[5-8] chemicals and heavy metals,[9-15] pathogens[16-22] and stress.[23-25] Diabetics are instructed to eat low-glycemic foods; however, certain healthy foods might contribute to diabetes in some individuals. Cow's milk casein was shown to cross react with insulin autoantibodies.[5-6] The antibodies against a variety of low-glycemic foods, such as zucchini, seaweed, tilapia, garbanzo beans (chickpeas) and peanuts, were shown to cross-react with pancreatic islet cell antigens.[7] In some individuals with immune dysfunction, a common trait among patients with T2D, cross-reactivity between food antigen antibodies and pancreatic tissues may occur. Indeed, in a previous study on randomly selected patient test results from patients tested simultaneously for tissue and dietary protein reactions, patients with antibodies to wheat/gluten proteins, cow's milk dairy proteins and/or lectin/agglutinin proteins also made antibodies against glutamic acid decarboxylase-65 (GAD-65) 22%, 17% and 16% respectively.[8] This cross-reactivity can exacerbate diabetes.

Chemicals and heavy metals have been shown to affect some people with T2D.[9-12] Bisphenol-A, a known endocrine-disrupting chemical, interferes with cell signaling pathways involved in weight and glucose homeostatis,[13] while phthalates, combined with a high fat-diet, aggravated glucose intolerance, insulin tolerance and insulin resistance and induced lesions in the pancreas and kidneys in rats.[10] Heavy metals such as nickel and mercury also exacerbate diabetes. Nickel exposure can induce hyperglycemia, possibly due to its effect on pancreatic glucagon and decreasing peripheral utilization of glucose,[14] while exposure to mercury can cause irregular pancreatic islet cell function.[15]

The role of pathogens in T2D was eloquently reviewed by Casqueiro et al, in 2012.[16] Because patients with diabetes more often have immune suppression via reduced T cell response, neutrophil function, and disorders of humoral immunity,[17-18] they are more susceptible to infections and have more severe reactions. During the recent SARS-CoV-2 pandemic leading to COVID-19, having diabetes meant higher risk for infection, severity and morbidity compared with individuals who are not diabetic.[19] Patients with T2D can host a variety of pathogens, from *Porphyromonas gingivalis* to *Staphylococcus aureus*, which can be harbored in multiple locations including the lungs, gastrointestinal tract, urinary tract and liver. Furthermore, antibodies against pathogens such as *Helicobactor pylori*, rotavirus and cytomegalovirus, were shown to cross-react with pancreatic elements.[20-22]

PFM models include protocols for stress management and restorative sleep, 2 problem areas for patients with T2D. Stress can be both a cause and a consequence of diabetes.[23] Psychosocial and socioeconomic stressors have been associated with the development of obesity, T2D and other chronic disorders. The pathophysiology of stress-induced T2D is still being investigated; however, epidemiological studies show a link between stress and diabetes.[24] Stress management and perceived social support can lead to a reduction in the HbA_{1c} levels in patients with diabetes.[25] One stressor for many people is the lack of quality sleep. Epidemiologic studies, noted by Knutson et al in 2006, found that a correlation between short duration or poor quality sleep may increase the risk for developing T2D.[26] In a rodent study on circadian rhythms, a disrupted light-dark cycle resulted in altered rhythms in body temperature, greater body weight gain, hyperleptinemia and hyperinsulinemia, as seen in metabolic syndrome.[27]

PFM addresses imbalances, dysfunctions, burdens and deficiencies in a mind, body, spirit approach. When we applied this model to our patients with T2D, we began to see better outcomes as evidenced not only in T2D biomarkers, but also by the reduction in diabetes-related medications needed. After the article by Wang et al.[19] regarding COVID-19-related severity in people with T2D was published, we contacted our 11 patients to ask how well each handled the pandemic that was raging in the geographic area of the clinic. Of the patients, 5, including the 2 oldest patients, reported no COVID-19 infection. The youngest person in the group had been infected with COVID-19, but had not been hospitalized. The remaining 5 patients did not respond. Although many factors may be involved here, we are confident that the lifestyle changes implemented in this group of patients with T2D improved their immune systems and allowed them to beat the odds against them.

Limitations

The weaknesses of this study include the lack of results from patients with T2D treated only with allopathic medicine for comparison; the single geographic area limits the universal effectiveness of the PFM model; the small number of study participants.

This small study provides a step toward larger, broader studies that incorporate the PFM model in the management of patients with T2D.

CONCLUSIONS

As more research shows the diversity in pathologies involved in T2D, the greater the need for the same diversity in treatment protocols in the management of individuals with T2D. Our small study shows that the PFM model, which incorporates a multifactorial evaluation of the individual patient, is an effective way to manage patients with T2D. Our strongest evidence is the elimination or reduction of diabetes-related medication.

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