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A Retrospective Analysis of HbA1c Reduction in Type 2 Diabetes Using Precision Nutrition Supported by Digital Twin Technology

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Abstract

Objective: The purpose of this study was to compare baseline measurements with those following 90 days of participation in the Twin Precision Nutrition (TPN) Program made possible by Digital Twin Technology to assess changes in hemoglobin A1c (HbA1c), anti-diabetic medication use, insulin resistance, and other ambulatory glucose profile metrics**.**

Method: Patients with type 2 diabetes who took part in the TPN Program and had at least four months of follow-up were included in this retrospective analysis. In order to generate recommendations that would allow specific patients to avoid foods that cause blood glucose spikes and to replace them with foods that do not, the TPN machine learning algorithm employed daily continuous glucose monitor (CGM) and food intake data. Doctors who had access to daily CGM data adjusted prescription dosages and kept track of patients' status.

Results: All analyses were conducted on the 100 patients who stuck with the TPN Program for at least 80 days out of the 180 patients who first signed up for it. During the 80-day follow-up evaluation, the mean (standard deviation) HbA1c had declined from 8.7±2.1% to 6.8±1.0% at baseline, the mean weight had decreased from 79.1±16.1 kg to 74.1±14.6 kg, and the mean fasting blood glucose had decreased from 151.1±45.1 mg/dl at baseline to 129.0±36.6 mg/dl. The HOMA-IR (homeostatic model evaluation of insulin resistance) score was dropped by 56.8%, from 7.3 to 3.1. At the 80-day follow-up assessment, all 11 patients who were on insulin had stopped taking this medication; 37 of the 55 patients taking metformin had stopped metformin; 25of the 27 patients on dipeptidyl peptidase-4 (DPP-4) inhibitors discontinued DPP-4 inhibitors; all 12 patients on alpha-glucosidase inhibitors discontinued these inhibitors; all 33 patients on sulfonylureas were able to stop taking these medications; two patients stopped taking pioglitazone; all ten patients on sodium-glucose cotransporter-2 (SGLT2) inhibitors stopped taking SGLT2 inhibitors; and one patient stopped taking glucagon-like peptide-1 analogs

Conclusion: The findings show that patients with type 2 diabetes can benefit from daily precision dietary counseling based on CGM, food consumption data, and machine learning algorithms. Patients who followed the TPN Program for 4 months saw their HbA1c drop by 1.8 percentage points, their weight decrease by 6.0%, their HOMA-IR reduce by 56.8%, their glucose time below range significantly decrease, and, for the majority of patients, their need for diabetic medication disappear.

Keywords: Artificial intelligence, continuous glucose monitoring, stopping diabetes medication, digital twin technology, lowering hemoglobin A1c, and precision diet

Introduction

The chronic condition known as type 2 diabetes (T2D) has always been seen as incurable. Improvement in the disease's symptoms and a slowing of its course are frequently the best results hoped for [Figure 1; 1]. Usually, as a condition progresses, the need for glucose-lowering medicine, medical expenses, and consequences rise [2]. The World Health Organization's 2016 global report on diabetes recognized that calorie restriction and weight loss can reverse diabetes [3]. It is generally agreed that maintaining haemoglobin A1c (HbA1c) below 6.5% for an extended period of time without using insulin or oral hypoglycemic medications (with the possible exception of metformin) would be considered diabetes reversal or remission [1, 4], even though specific criteria have not been finalised.

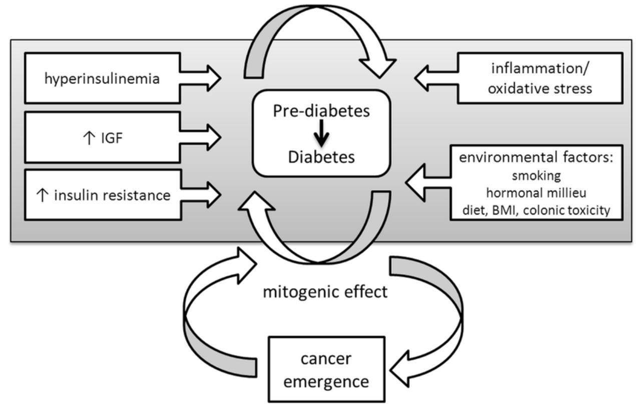

Figure 1: T2DM and its progression.

Bariatric surgery, low-calorie diets, and carbohydrate restriction have all been shown in several studies to reduce weight and improve glycemic control [1, 5]. Bariatric surgery has some restrictions that could prevent its usage, including a high cost for the procedure and a higher chance of adverse effects [1]. The drawback of utilising a low-calorie diet to manage diabetes is that it might not be long-term maintainable [2]. Studies employing carbohydrate restriction discovered better glycemic control, but frequently only employed brief trials, only included small groups, concentrated on patients who were morbidly obese, and/or excluded participants who were on insulin [2, 6–10].

Despite the significance of maintaining proper glycemic control and the link between postprandial glycemic response (PPGR) and complications of diabetes, predicting the effect of particular foods on PPGR has proven difficult due to the wide variation in how different people react to the same food [11]. There have been some attempts to determine PPGR using meal carbohydrate content [11] or glycemic indexes [12]. Several research [11, 13, 14] have attempted to develop or test PPGR prediction models based on the specific items consumed during individual meals. To present, no research have attempted to reverse diabetes using long-term continuous glucose monitoring (CGM), artificial intelligence techniques, and precision diet.

The Twin Precision Nutrition (TPN) Program feeds specific data on the patient's food consumption and CGM readings into a machine learning predictive model, which then outputs recommendations for the patient's daily precision nutrition. Examining changes in HbA1c, anti-diabetic drug use, insulin resistance, and other ambulatory glucose profile (AGP) measures between baseline and after 80 days of TPN Program participation in individuals with T2D was the goal of this study. Every indicator was expected to improve significantly over the course of the 90-day treatment period.

METHOD:

Study Design: This was a retrospective analysis carried out in SRS Diabetes Speciality Care.

Methodology: The TPN Program is an outpatient program that makes use of whole-body Digital Twin Technology, powered by artificial intelligence and the Internet of Things, to comprehend the metabolic impairment in the patient's body, which varies depending on the patient. The platform tracks and analyses the body's health signals in order to tailor the patient's care by gathering data through body sensors and a mobile app. Each patient's clinical history, vitals, EKG, and biothesiometry were evaluated during their first TPN Program enrollment appointment. At the beginning of treatment, 20, 50, and 80 days later, fasting blood samples were taken. Each patient received support from a health coach to help with the TPN Program. During enrollment, the patient's age, gender, amount of diabetes, and body mass index (BMI) were noted. HbA1c (%) served as the study's main outcome.

Sample size: 100 patients diagnosed with T2D who opted to engage in the TPN Program for 80 days and who were at least 61% adherent to program procedures.

Inclusion Criteria: In order to participate in the study, program participants had to have an adequate hepatic and renal function, with the former being defined as serum aspartate transaminase or alanine transaminase ratio B 3 fold the upper limit of normal, and the latter being defined as serum creatinine B or an estimated glomerular filtration rate.

Exclusion Criteria: Patients were disqualified if they had a history of ketoacidosis, severe psychiatric illnesses, or if they had recently suffered a myocardial infarction, a stroke, or angina.

Statistical Analysis: Means and standard deviation were used to characterise continuously varying descriptions (SD). To report the means of binary variables, percentages were employed. Pairwise t-tests were used to analyze changes in the mean values of continuous variables from the baseline to 20, 50, and 80 days following enrollment. Paired sign tests were used to assess changes in medians. The Mc Nemar chi-squared test was used to analyze changes in the average values of binary variables.

Results

180 patients in all were signed up for the TPN Program. Among these, 20 patients left the programme prior to the completion of the 80-day follow-up period due to challenges performing the study-related procedures (such as wearing the CGM for an extended amount of time) or because of unanticipated life-changing circumstances, such as family emergency. 60 of the 160 patients that remained were not included in the analysis because they exhibited flagrant disregard for the TNP Program's nutritional recommendations. 29.6% of the

100 patients who stuck with the TPN Program were female. The 100 patients were enrolled with an average (SD) age of 52.3 (10.1) years, a T2D duration of 8.3 (6.4) years, an average BMI of 29.1 (5.7) kg/m^2, and an insulin use rate of 18.8%.

At baseline, the mean (SD) HbA1c of the 100 patients was 8.7% (2.1%); at 20 days, it was 7.6% (1.5%); and at 50 and 80 days, it was 6.8% (1.0%). (all p<0.0002 vs. baseline). 9.3% of patients had baseline HbA1c levels below 6.5%. At 20 days, 38.1% at 50 days, and 39.6% at 80 days, the proportion of patients with measured HbA1c 6.5% rose to 24.5%, 38.1%, and 39.6%, respectively (all p<0.002 vs. baseline). Over the course of the trial, the eA1c also dropped dramatically, from 6.8% (2.2%) at baseline to 5.6% (1.1%) at 20 days, 5.7% (1.0%) at 50 days, and 5.8% (1.1%) at 80 days (all p <0.002 vs. baseline).At baseline, the patients' mean body weight was 79.1(16.1) kg; at 20 days, 76.0 (15.2) kg; at 50 days, and at 80 days, 74.1 (14.6) kg (all p<0.0002 vs. baseline).

At baseline, the mean (SD) FBG was 151.1 (45.1) mg/dl; at 20 days, it was 135.1 (38.0) mg/dl (p = 0.0042); at 50 days, it was 131.5 (31.9) mg/dl (p = 0.0204); and at 80 days, it was 129.0 (36.6) mg/dl (p = 0.0003). After 80 days on the TNP Program, 59.6% of patients had FBG 125 mg/dl, compared to 34.4% of patients at the baseline. From 7.3 (3.4) at baseline to 3.0 (2.4), 3.2 (2.3), and 3.1 (2.7) at 80 days (all p<0.0001 vs. baseline), the mean HOMA-IR (SD) decreased. There was a 56.8% decrease from baseline to 80 days.

From 147.3 (59.0) mg/dl at baseline, the mean (SD) glucose levels recorded by CGM decreased to 116.6 (27.8) mg/dl at 20 days, 120.4 (29.5) mg/dl at 50 days, and 122.5 (33.2) mg/dl at 80 days (all p<0.002 vs. baseline). The mean C-peptide levels also dropped from 3.1 (2.1) ng/ml at baseline to 1.6 (0.8) ng/ml at 20 days, 2.0 (0.8) ng/ml at 50 days, and 1.8 (0.9) ng/ml at 80 days (all p<0.0002 vs. baseline). Large drops in the C-peptide levels of individuals with extremely high baseline levels contributed to some of this decrease by bringing their levels closer to normal.

The improvement in the average amount of sleep per night was not statistically significant, but the mean (SD) thenumber of daily steps went from 4677.3 at the beginning to 7004.2 after 80 days (p <0.0002). At 80 days, the median resting heart rate dropped from 75.1 bpm at baseline to 71.1 bpm (p <0.0002). The average daily calorie intake dropped from 1884.1 kcal at the beginning of the study to 1649.5 kcal after 20 days, 1607.3 kcal after 50 days, and 1573.1 kcal after 80 days. In the program's first week, 54 patients had TIR levels lower than 71%. In 80 days, 57 patients had TIR levels [than 71%], and this outcome was kept.53 patients in the first week of the treatment had TIR levels that were under 70%. 56 patients had TIR levels [more than 70%] after 80 days, and this result was maintained.

In just one patient during the first week of the programme was the percentage of time [150 mg/dl (TAR level 2 of 11.8%) greater than the approved threshold (4%) [17]; this was subsequently decreased to 0.4% at the conclusion of 4 months of treatment. Initial TAR level 1 values for 3 patients were higher than the acceptable threshold (24%) [17]; these values decreased from 41.6 and 71.2% during the first week to 2.1 and 15.7%, respectively, after 4 months.

By the end of the first week of the TNP Program, the mean TAR level 2, TAR level 1, and TIR readings had returned to normal ranges, and they stayed there for the entire 80-day follow-up period. The mean (SD) TIR started at 87.0% (16.7%) in the first week and stayed the same for the remaining 80 days before reaching 87.0% (19.3%). In the first week and at 80 days, the mean TBR level 1 readings were just slightly over the normal range. Mean TBR level 2 readings were somewhat above average during the first week, but after 80 days, they had reduced even more to be well within the usual range (**Table 1)**.

Table 1: Metrics for continuous glucose monitoring during week 1 and 80 days afterwards

Continuous glucose monitoring metrics	TNP Program Week 1			80 Days of follow-up		
	Normal Range	N	Mean (SD)	N	Mean (SD)	P-value vs 1 week
Blood glucose % time above 150 mg/dl (TAR level 2)	<4	100	0.4 (1.5)	100	1.7 (10.4)	0.3188
Blood glucose % time above 170 mg/dl and B <150 mg/dl	<24	100	4.7 (11.1)	100	5.7 (9.3)	0.5296
Blood glucose % time in range 60–170 mg/dl (TIR)	>71	100	81.0 (16.7)	100	87.0 (19.3)	0.9978
Blood glucose % time below 60 mg/dl and >44 mg/dl (TBR level 1)	< 3	100	6.1 (11.8)	100	5.1 (14.3)	0.6135
Blood glucose % time below 44 mg/dl (TBR level 2)	<2	100	1.3 (3.1)	100	0.2 (0.7)	0.0055

There were no cases of diabetic ketoacidosis observed. Both new occurrences of gout and episodes of symptomatic hypoglycemia were not recognised or reported. Throughout the research, there were no additional severe adverse events. Non-serious adverse effects that were brief and early in the research included headaches, exhaustion, and constipation.

Discussion

In order to help each patient with T2D avoid foods that cause blood glucose spikes and replace them with foods that do not, the TPN Program integrates CGM, Internet of Things technology, food intake data, and machine learning algorithms to deliver daily precision nutrition recommendations. The findings of the study support the claim that during the course of the program's 80 days, every diabetes-related outcome was considerably improved. The findings of the current study are comparable to those of earlier studies on interventions in populations of diabetic patients.

Research on bariatric surgery has demonstrated that most patients can reach normal HbA1c and glucose levels after surgery, often in just a few days [1, 18]. Very low-calorie diets have been shown to significantly lower glucose and HbA1c levels as well as the need for insulin, according to studies [1, 19]. However, other trials on low-calorie diets have also discovered that patients have trouble sticking to them, and the improvements in diabetic endpoints could not be sustained over the long run [20–23].In the current trial, all insulin-using individuals stopped using it, along with the majority of oral diabetes treatments. When isocaloric diet was resumed after 10 weeks in the very low-calorie research by Steven et al. [19], 40% of patients reached FBG 126 mg/dl (the criterion for partial remission of diabetes [24]), and 43% of patients still had it at 6 months.

In a trial of morbidly obese diabetic patients on a low-carb diet, the HbA1c of these patients dropped from 7.6 to 6.6% in 10 weeks [2]; at this time, the proportion of participants with HbA1c 6.5% had grown from 20 to 56%, and 57% had reduced or stopped taking one or more diabetes medications [2]. Within a year, these patients' HbA1c levels had decreased to 6.3%, 94% had ceased using insulin, and 100% had stopped using sulfonylureas [5]. In a 12-week study of T2D patients on a low-carb ketogenic diet [7], HbA1c declined and FBG dropped from 178.1 to 156.4 mg/dl.

It has been demonstrated that lower HbA1c and HOMA-IR values are associated with lower health risk in diabetic individuals. According to Stratton et alresearch, .'s diabetic microvascular consequences are reduced by 37% when HbA1c levels are reduced by just 1.0% [25]. Lower HOMA-IR readings independently predicted decreased cardiovascular disease prevalence and incidence, according to Bonora et al. [26]. Moreover, it has been demonstrated that lower TBR and higher TIR (even by just 5%) are related to reduced problems from diabetes [17]. TIR and HbA1c have a strong positive correlation, and each 10% increase in TIR results in a 0.4–0.8 percentage point decrease in HbA1c [27, 28]. Moreover, it has been demonstrated that with every 10% decrease in TIR, the risks for developing retinopathy and microalbuminuria rise by 64 and 40%, respectively [29]. Similar to this, a post-hoc analysis of the data from the Diabetes Control and Complications Study revealed a connection between TBR glucose thresholds of 54 mg/dL and 70 mg/dL with an elevated risk for severe hypoglycemia [30].

Conclusion

The findings show that patients with T2D can benefit from daily precision nutrition recommendations based on CGM, Internet of Things technology, food intake data, and machine learning algorithms. The 100 participants who followed the TNP Program for 80 days saw a considerable improvement in their diabetes-related outcomes. After completing the TPN Program for 4 months, patients' HbA1c levels dropped by 1.8 percentage points, their HOMA-IR levels dropped by 56.8%, their TBR levels significantly dropped, and the majority of patients stopped taking their diabetes medications. Continuing outcomes will provide more information about the long-term viability, security, and sustainability of the TNP Program.

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