

Long-term remission of type 2 diabetes through intense lifestyle modification program – A case series

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ABSTRACT

Type 2 diabetes (T2D) remission is being widely accepted and documented as feasible through calorie restriction and bariatric surgery. Recent studies with lifestyle changes have also shown T2D remission; however, long-term remission through lifestyle modifications is not yet established. Though glycated hemoglobin (HbA1c) is a universally accepted indicator of glycemic status, oral glucose tolerance test (OGTT) would be a more robust marker in understanding whether the metabolic abnormalities in glucose metabolism have undergone complete remission as well. We present a case series of four patients enrolled in the Holistic Transformation Program, a lifestyle modification program, between 2016 and 2018. The intervention was a combination of a vegan diet, structured exercises, and stress management delivered over 12 months. All four patients successfully achieved T2D remission and cleared OGTT consecutively for a minimum period of 3 years. Our findings suggest that long-term T2D remission may be possible through lifestyle modification.

Keywords: Diabetic remission, exercise, lifestyle changes, vegan diet

Introduction

Type 2 diabetes (T2D) remission is widely reported globally. The chronic and progressive nature of T2D demands long-term medical attention to reduce the risk of microvascular and macrovascular complications.^[1] Even intense interventions only effectively delay the progression of complications,^[2] and the best way to prevent the complications is possibly through T2D remission. The earlier documented evidence on T2D remission was primarily of surgical interventions such as bariatric surgery.^[3] However, more recent evidence suggests

that nonsurgical lifestyle interventions such as a very-low-calorie diet (VLCD),^[4] intermittent fasting,^[5] and structured lifestyle modifications could bring about effective T2D remission.^[6,7] T2D remission is defined as glycated hemoglobin (HbA1c) levels of <6.5% over a continuous period of 3 months without any antidiabetic medications. Though HbA1c is a universally accepted indicator of glycemic status, oral glucose tolerance test (OGTT) would be a more robust marker in understanding whether the metabolic abnormalities in glucose metabolism have undergone complete remission as well. Most T2D patients receive treatment in primary care, either in family medicine (FM) or in general internal medicine (GIM) or from an endocrinologist. Research to date shows that FM providers vary from GIM in terms of beliefs, attitudes, and practice choices when it comes to managing T2D, but this limited literature is inconsistent. The current case series presents four patients who underwent complete T2D

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remission (as per the above definition) following a structured Holistic Lifestyle Transformation Program (HTP) and had also successfully cleared the OGTT continuously for a period of 4 years or more during the follow-up.

Case Presentation

Our case series involves four patients [see Table 1]. All patients were diagnosed with T2D and were on oral hypoglycemic agents (OHAs) at the time of joining the program. None of the patients cleared the OGTT at the time of enrollment. Annual follow-up checkups were performed for all four patients.

Patient 1 is a 72-year-old male (68 years old at the time of joining the program in 2016, with T2D for 6 years along with hypertension). Diabetes medications at the time of enrollment were a combination of sitagliptin (50 mg) and metformin (1000 mg) once daily. He lost 11.1 kg body weight (14.9%) during the 1 year and his medication was stopped within 12 days of starting the program based on the daily blood sugar level monitoring. He appeared for his first OGTT post-remission in 2016, 5 months after becoming free from medicine, and cleared OGTT every year till 2021.

Patient 2 is a 42-year-old female (36 years old at the time of joining the program in 2016, with T2D for 1 year). Diabetes medication at the time of admission was glimepiride 0.5 g once daily. Her body weight loss was significant, as she lost 19.5 kg body weight (25.3%) during the 1 year, and her medication was tapered down and stopped in 45 days. She appeared for her first OGTT in 2017 and cleared OGTT every year till 2021.

Patient 3 is a 68-year-old male (64 years old at the time of joining the program in 2018, with T2D for 4 years). Diabetes medications during enrollment were glimepiride (2 mg), metformin (500 mg), and voglibose (0.2 mg) combination twice daily and repaglinide (0.5 mg) once daily. He lost 6.8 kg body weight (9.4%) during the 1 year, and his medication was tapered down and stopped in 42 days. He appeared for his first OGTT post-remission in 2018 and cleared OGTT every year till 2020.

Patient 4 is a 52-year-old male (46 years old at the time of joining the program in 2016, with T2D for 12 years). Diabetes medication during enrollment was metformin 500 mg twice a day. He lost 14.1 kg body weight (16.3%) during the 1 year, and

his medication was tapered down and stopped in 90 days. He appeared for his first OGTT post-remission in 2016 and cleared OGTT every year till 2021.

Intervention details

The 1-year (6 months of intervention and 6 months of follow-up) intense lifestyle modification program (HTP) is a combination of a plant-based vegan diet, physical activity, medical support, and psychological support (for stress management). The intervention includes a customized vegan diet to meet everyday dietary micro- and macronutrient requirement, a structured physical activity regimen (including antigravity exercises, yoga poses, and aerobic practices), medical management, and stress management support (through psychological counseling and mindfulness meditation). Patients are encouraged to achieve the desired body mass index (BMI). One hour of exercise is advised daily, which is individualized for patients through live in-person or online sessions to improve the stagnant lymphatic circulation and muscle strengthening. Educational sessions for patients are organized to make them aware of diabetes and its management.

Regular monitoring of the protocol implementation by the patient was done through telephonic or personal appointments with a medical expert. The dosage of the diabetes medication was monitored and adjusted on a need basis by the assigned doctor through daily updates of blood glucose levels. After tapering the medications, the patients were instructed to reduce the frequency of reporting and encouraged to take the consultation once in every 3 months. They were monitored till the end of the program even after discontinuing the diabetes medications.

After being medication free for a minimum duration of 5 months, the patients attempted their first OGTT. Based on the American Diabetes Association (ADA), fasting and 2-h plasma glucose levels are considered the gold standard test for diagnosing diabetes mellitus. All patients had HbA1c <6.5 before attempting OGTT. For the OGTT, a fasting blood sample was collected to establish a baseline glucose level. The patients were then given 75 g (recommended dosage for OGTT by WHO) of dextrose monohydrate in 250 ml of water. A second blood sample was collected after 120 min (postprandial [PP]) of consuming the glucose. Based on the OGTT results, the patients were categorized as “cleared OGTT” if the fasting blood glucose level was <100 mg/dl and the PP was <140 mg/dl.^[12]

Table 1: Baseline and follow-up data of patients

Patient	Present age (years)	Sex	Duration of diabetes	Diabetic medication at baseline	Frequency ^a	Weight (kg)			BMI (kg/m ²)			HbA1c (%)	
						B	P	F ^b	B	P	F ^b	B	P
1	72	Male	6 years	Sitagliptin (50 mg) + metformin (1000 mg)	0–0–1	74.5	63.4	58	27.4	23.3	21.3	5.8	5
2	42	Female	1 year	Glimepiride 500 mg	1–0–0	77.1	57.6	56.3	30.1	22.5	22	7.7	5.1
3	68	Male	4 years	Repaglinide 0.5 mg Glimepiride (2 mg) + metformin (500 mg) + voglibose (0.2 mg)	1–0–0 0.5–0–0.5	72.2	65.4	65.2	23.9	21.6	21.6	8.5	6.2
4	52	Male	12 years	Metformin 500 mg	0–0.5–1	86.1	72	74.9	30.3	26.1	26.4	6.9	5.7

B=at baseline, BMI=body mass index, HbA1c, glycated hemoglobin, P=post-1 year of intervention. ^aThe dosage and timing of the medication (morning–afternoon–night). ^bFollow-up data as of December 2021

Results

All four patients successfully cleared OGTT. Similarly, the HbA1c values of all four patients reduced to less than 6.5% without any diabetes medications, and thus, they achieved remission as per definition.^[8] Body weight is documented to be one of the important components facilitating T2D remission, and all four patients had significant weight reduction as well during the 1-year intervention period, with weight loss percentage varying between 9.4% and 25.3% from baseline [see Tables 1 and 2].

Discussion

There are three major outcomes which we would like to highlight. They are 1. OGTT clearance, 2. HbA1c normalization, and 3. weight loss.

To our knowledge, this is the first documented evidence of T2D remission along with clearance of OGTT. A joint review by the Association of British Clinical Diabetologists and the Primary Care Diabetes Society examined evidence to support the theory of T2D remission. The primary evidence was in the form of studies in patients with T2D undergoing bariatric surgery and studies involving lifestyle modifications, which indicated that both could result in a partial or complete cessation of glucose-lowering drugs. Two major reasons attributed to successful diabetes remission were significant weight loss and a shorter duration of diabetes.^[9] Though significant weight loss was observed in all four patients, the duration of diabetes since diagnosis ranged between 1 and 12 years.

A recent study in newly diagnosed T2D patients showed that remission is possible through intensive lifestyle modification and

if weight regain is avoided, remission could be sustained. Only a few studies have carried out long-term follow-ups^[10,11] with an average duration of 2–5 years, showing sustained remission based on sustained weight loss and HbA1c levels (<6.5) after the withdrawal of OHAs. A recent review suggests that although HbA1c is a valuable tool for the diagnosis of dysglycemia, its reliability to screen high-risk individuals is questionable when compared to the information derived from OGTT.^[12] Our study shows not only sustained weight loss and optimal HbA1c levels, but also the ability of a patient previously diagnosed with T2D to process 75g of glucose through clearance of the OGTT successfully for 3 or more years.

Conclusion

Structured HTP helps in T2D remission and successfully clearing OGTT. The remission could be attributed to the significant weight loss observed in all the patients. A randomized controlled trial with an adequate sample size would help validate our observations.

Patient consent

Written informed consent for publication of their clinical details was obtained from all the patients.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Table 2: OGTT results of the patients

Patient No	Outcome variable	OGTT first attempt	OGTT second attempt	OGTT third attempt	OGTT fourth attempt	OGTT fifth attempt	OGTT sixth attempt
Patient 1	Year	2016	2018	2019	2020	2021	-
	HbA1c (%)	5.3	5.5	5.5	5.3	5.4	-
	Fasting BSL (mg/dl)	87	95	70	91	94	-
	2-h BSL (mg/dl)	109	128	58	132	108	-
	OGTT status	Cleared	Cleared	Cleared	Cleared	Cleared	-
Patient 2	Year	2017	2018	2019	2020	2021	-
	HbA1c (%)	4.8	4.8	4.9	4.9	5.1	-
	Fasting BSL (mg/dl)	83	85	87	98	87	-
	2-h BSL (mg/dl)	126	99	111	112	97	-
	OGTT status	Cleared	Cleared	Cleared	Cleared	Cleared	-
Patient 3	Year	2018	2019	2020	-	-	-
	HbA1c (%)	6.1	6	6.3	-	-	-
	Fasting BSL (mg/dl)	94	85	99	-	-	-
	2-h BSL (mg/dl)	100	75	86	-	-	-
	OGTT status	Cleared	Cleared	Cleared	-	-	-
Patient 4	Year	2016	2017	2018	2019	2020	2021
	HbA1c (%)	5.6	6	5.6	5.8	5.6	5.6
	Fasting BSL (mg/dl)	96	97	80	96	91	91
	2-h BSL (mg/dl)	87	124	98	139	126	100.5
	OGTT status	Cleared	Cleared	Cleared	Cleared	Cleared	Cleared

2h=2 h postprandial, BSL=blood sugar level, HbA1c=glycated hemoglobin, OGTT=oral glucose tolerance test, OHA=oral hypoglycemic agent, OGTT

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Conflicts of interest

There are no conflicts of interest.

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