

Commentary

Reversal of Type 2 Diabetes Mellitus

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Management of type 2 diabetes mellitus (T2DM) is an art; as it entails a balance between managing plasma glucose levels and preventing its complications. The emergence of the concept of 'reversal of diabetes' might offer a big stride in our existent treatment algorithm. This novel approach focuses on long-term, significant control of plasma glucose levels in T2DM patients. Reversal of diabetes can be considered when the target HbA1c of <6 gm% for glycemic control is achieved in T2DM patients without the use of any medications.

T2DM has long been identified as an incurable chronic disease and the best achievable outcome has been the amelioration of symptoms of hyperglycemia or slowing down of disease progression that is otherwise inevitable. Consequent to the pathological changes in long-standing T2DM, the functions of pancreatic beta-cells decline linearly with time. Approximately 50% of T2DM patients need insulin therapy within ten years of their initial diagnosis.¹ Overall, there is strong evidence that T2DM is a progressive disease; therefore, insulin therapy is eventually required to maintain reasonable glycemic control and prevent further diabetic complications.

However, recent developments suggest the possibility of 'reversal of diabetes' through dietary changes, physical exercise, and weight loss. Henceforth, it is possible to attain the target plasma glucose level without medications. In the early stage of T2DM, insulin resistance, leading to insulin deficiency is responsible for hyper-glycemia. In an average healthy person, insulin is responsible for increasing the uptake of carbohydrates in the liver, muscles, and other target organs. In an obese person, there is the deposition of high visceral and subcutaneous fat at insulin targeted sites. Hence, insulin does not work efficiently at the target site, and glucose level is not reached at the target level. The critical point for reversing diabetes is to reduce this visceral and subcutaneous fat through a low-calorie diet, physical exercise, bariatric surgery,

fasting, etc.

It has been well proven that diabetes can be completely resolved following bariatric surgery.² After bariatric surgery, plasma glucose levels are normalized within a few days of the surgery, even without any significant reduction in body weight. This is mediated largely by the altered secretion of incretin hormones.^{3,4} Post-bariatric surgery, a sudden negative energy balance is observed in the metabolism. The reduced fatty acid concentration in hepatocytes leads to a decreased export of triacylglycerol lipoprotein to the pancreas and beta cells, which was also released subsequent to the chronic inhibitory effect of excess fatty acid exposure.⁵

Further, fasting plasma glucose level is determined by hepatic glucose production (gluconeogenesis and glycogenolysis), and hepatic insulin sensitivity increases with a reduction in intrahepatic lipid content.^{6,7} A study suggests that intrahepatic fat content is decreased subsequent to a moderate reduction in body weight.⁸ Petersen et al⁸ observed that after eight weeks of moderate energy restriction in patients with T2DM, liver insulin sensitivity improved without any significant change in muscle insulin sensitivity. A deficient energy intake in healthy obese individuals has been observed to lower liver fat content within days.⁹

Considering these observations, the key factor to reversing diabetes seems to be weight loss and physical activities. Sometimes losing a specified weight could help patients live diabetes-free, especially if the disease is not long-standing (a few years) and also when insulin has not been initiated yet. Reversal of diabetes can also be easily attained without much strenuous effort in an early prediabetic state. Hence, a determined and focused attitude can help people reverse T2DM, which may eventually result in an astonishing improvement in the overall physical and mental health of the patients.

According to the initial clinical research, the effective ways to reverse diabetes include exercise, low carbohydrate diets, very low calorie, fasting, and bariatric surgery.

Low-Carbohydrate Diet

Diet with lower carbohydrate content requires less insulin for their metabolism, resulting in less insulin resistance. Higher insulin secretions predispose the target organ to more insulin resistance. Further, elevated plasma glucose levels can destroy the insulin-secreting pancreatic beta cells, aggravating hyperglycemia. A research study suggests that a low-carbohydrate diet could achieve significant reversal rates in patients with T2DM.⁹

Very Low-Calorie Diet (VLCD)

A very low-calorie diet can be associated with a significant weight reduction and improvement in insulin resistance allowing patients with T2DM to wean off their diabetes medication. A study reported that an 800 kcal per day diet for eight weeks can cause remission from T2DM in nearly 65% of patients.¹⁰ A very low-calorie diet for 2-3 weeks is also commonly advised before bariatric surgery to reduce visceral and liver fat mass, minimizing peri and post-surgical complications.¹¹ The reversal of diabetes appeared to be correlated with a significant reduction in fat storage in the liver and pancreas. A VLCD is an extreme form of the diet with a very low calorific value and should be used carefully. It necessitates the supervision of professional and strict control of calorie intake by the patient. A VLCD diet offers good weight and plasma glucose control, thereby providing strong motivation toward long-term compliance. It should be started as early as possible after diagnosis.

Exercise

Diabetes can also be managed by physical activity, but remission of elevated plasma glucose levels and weight reduction can not be achieved easily with workouts alone. A modest lower-calorie diet and a significant escalation in exercises to burn calories are essential for a successful remission.

In a study, T2DM patients taking 10,000 steps a day and at least 2½ hours of moderate exercise a week were observed. The reduction in 500-750 calories per day with medication adherence could lead to reaching normal plasma glucose without medication in more than half individuals.¹² Exercise has a significant impact on preventing and controlling insulin resistance, prediabetes, gestational diabetes mellitus, T2DM, and diabetes-related health

complications. Both aerobic and resistance training improve insulin action and can assist in managing plasma glucose levels, lipids levels, blood pressure, cardiovascular risks, mortality, and quality of life. However, regularity is essential in exercise for continued benefits and most likely includes regular training of varying types. It is weight loss as a consequence of exercise and calorie restriction that matters.

Bariatric Surgery

This is a type of gastrointestinal surgery that helps lose weight by altering the stomach and digestive system to limit how much the patient can eat. Bariatric surgery is generally a treatment of choice in severe obesity (when BMI is 35 or higher).

Besides helping to lose weight, it may also help reverse diabetes in some other ways, although the exact mechanism is unknown. One theory suggests that bariatric surgery affects the hormones in the gut, which help control plasma glucose levels. The efficacy of T2DM reversal depends on the choice of the surgical procedure. Gastric sleeve surgery and gastric bypass have better long-term results than gastric banding. After the surgery, there is a unilateral improvement in glycemic control and in most cases, it is superior to the medical management of T2DM.

Subsequent to bariatric surgery or dietary restriction, there is a sequential occurrence of responses, ranging from a very early change in hepatic insulin sensitivity to a slower change in beta-cell function. These include:

1. Within seven days: fasting plasma glucose level and hepatic insulin sensitivity fall to normal within the first seven days of reduced energy intake. At this stage, intrahepatic lipid levels are also decreased by 30 from the baseline.
2. Within two months: Pancreatic fat is decreased, and beta-cell function is increased towards normal over the eight weeks of dietary energy restriction.
3. Within three months: After gastrointestinal surgery, the patient could gain 3.1 ± 1.0 kg body weight over 12 weeks. But their HbA1c remains steady because both the pancreatic and liver fat content do not increase.

In T2DM, there are abnormalities of both insulin secretion and insulin resistance. They both have a common etiology, i.e. excess lipid accumulation in the pancreas and liver, respectively.⁵ Clinical researchers estimate that in approximately 75% of patients, their T2DM can be reversed after bariatric surgery.

Fasting

Fasting can be a practical way to lose weight because it's reasonably straightforward, but it is not a mainstream treatment for T2DM. It has been reported that eating very few calories (500-600) two days a week and a normal diet for the other days helped people with T2DM lose weight and lower their plasma glucose levels.¹³

What Doesn't Work

When it comes to reversing diabetes, there is no magic pill. One should be cautious and beware of any such product that claims to cure diabetes or replace the currently prescribed diabetes medication. The FDA cautions that many illegally marketed products are unproven and possibly dangerous, including dietary supplements, over-the-counter drugs, alternative medicines, homeopathic products, and prescription drugs.

CONCLUSION

Additional evidence has emerged in recent years suggesting 'reversal of diabetes' as a possible alternative to be considered over conventional treatment and management of T2DM. The current standard of care may be suitable for some, but others may be given to choose the 'reversal of diabetes' approach, however, patient education, counseling and patient-centric discussions will play an utmost important role in such cases.

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