Commentary

Type 2 Diabetes reversal in India : Is a low carbohydrate diet practical and sustainable ?

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The root cause of type 2 diabetes mellitus (T2DM) is carbohydrate intolerance and insulin resistance. From a scientific perspective, our body doesn't need carbohydrates. While carbohydrate restriction per se can cut the cycle of glucose and insulin surges, it is "nutritional ketosis" that puts metabolic syndrome into reversal. Although variable from person to person, to get blood ketones above 1 mmol (optimal ketosis), it is typically required that one consumes less than 50 grams of carbohydrates/day. The typical recommendation is starting at 30 grams/day of carbs – a level that most people can consume and remain in nutritional ketosis, and at the same time affording us a wider range of food choices. In the context of a well-formulated Ketogenic diet, this level is safe, sustainable and satisfying. Once keto-adapted, depending on your metabolism and goals, one can incorporate slow release carbohydrate such as root vegetables, legumes etc.

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The root cause of T2DM is the combination of insulin resistance and carbohydrate intolerance. Carbohydrate intolerance occurs when more carbohydrates are consumed than one's tolerance level, which causes blood glucose to go high and stay higher for longer. Insulin is released in response to increases in blood glucose to help the glucose move to insulin sensitive tissues, where it can be used for energy or stored. Insulin resistance means that cells are resistant to the signal of insulin and stop responding - so most of the glucose stays in blood, leaving a situation with chronic high blood glucose. Chronic high blood glucose is the primary marker of T2DM and prediabetes, and to diagnose these conditions the glycosylated hemoglobin (A1c) test is used.

Widely held belief is that these diseases are caused by being overweight, eating too much fat, or not exercising enough - but because diabetes is by definition a disease of high blood glucose, the real underlying cause are conditions resulting in high blood glucose - the combination of excess carbohydrate intake along with carbohydrate intolerance or insulin resistance. While weight gain is associated with diabetes, it is an effect, not a cause - which is why there are diabetic patients who are never overweight. While exercise can help improve blood glucose, the lack of it is not the primary cause of high blood glucose.

In the last decade, oxidative stress and inflammation have been identified as key underlying causes of T2DM[1,2,3]. This is potentially transformative, because while T2DM has been known to be caused by insulin resistance, despite 50 years of intense research, no one has been able to pinpoint the root cause(s) of insulin resistance. Now we know that ketones at the normal levels characteristic of nutritional ketosis reduce oxidative stress and inflammation, and these benefits can be traced to the actions of genes we are all born with[4,5]. But without modest levels of circulating ketones, these inborn defences don't function properly. Stating this another way, eating a high carbohydrate diet turns off our defences against oxidative stress and inflammation, and this deactivation in turn contributes to (if not causes) insulin resistance. Furthermore, as noted above, the more dietary carbohydrates we consume, the greater the tide of glucose needing to be disposed of, which tends to further increased insulin resistance. It bears repetition that while carbohydrate restriction per se can cut the cycle of glucose and insulin surges, it is "nutritional ketosis" that reverses the essential pathophysiology of T2DM.

Human body requires many things in order to be healthy: sleep, water, micronutrients such as vitamins and minerals, as well as the macronutrients protein and fat. What it doesn't need, from a scientific perspective, is carbohydrates. This does not mean that blood glucose is unimportant but rather that blood glucose can be well maintained via metabolic processes such as gluconeogenesis without carbohydrates in a keto-adapted human.

While a plate of pasta may well be comfort food, it's

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not a power food. Human body will turn that simple carbohydrate into glucose rapidly, which will be burned by brain, muscles and other organs for a quick burst of energy, leaving a sensation of hunger and tiredness soon thereafter. And with underlying T2DM, pre-diabetes, or insulin resistance, body struggles to process the carbohydrate, leaving behind worsening glycemic control. Instead, a meal of grilled chicken and a salad full of healthy fats such as avocados, olives, nuts, cheese and ranch dressing, human body can fuel itself entirely on those nutrients without giving a post-meal glucose spike.

For somebody, who has been eating a typical Indian diet, his/her body is running primarily on carbohydrates. Besides carbohydrates, the average Indian diet also tends to be high in saturated fat, trans-fat (mostly related to widespread use of Vanaspati, a form of hydrogenated vegetable oil), and low in protein, cholesterol, monounsaturated fat (MUFA), and polyunsaturated fat (n-3 PUFA), and fiber[6].

But for somebody, who is facing medical problems stemming from processing carbohydrates, such as T2DM, prediabetes, insulin resistance, or metabolic syndrome, a low-carbohydrate approach can be life changing. As carbohydrates are strategically removed from diet, usually to an initial level of 30g per day, body will begin to run on fat as a fuel, both from ingested exogenous fat as well as endogenous fat from body stores. This adaptive process takes a few weeks to shift (typically 2-6 weeks) from carbohydrate-as-fuel to fat-as-fuel, during which liver will pitch in to produce glucose from protein in a process called gluconeogenesis.

The key to successfully—and sustainably—reducing carbohydrate intake to a level that body can effectively process is to replace those carbohydrate calories with a generous amount of healthy fats (such as olive oil, avocados, butter, and cheese) while consuming a standard, moderate amount of protein (from varied sources including meat, poultry, fish, eggs and nuts)

What Does the Term "Diabetes Reversal" Mean ?

- This is called "reversal" because most people can maintain blood glucose values below the diabetes range as long as they maintain a ketogenic diet. However, in most cases, if they return to a carbohydrate-rich diet, their diabetes will return. Thus this is a state of reversal, not a cure.
- The term "reversed" is used if average weekly fasting blood glucose values remain below 126 mg/dl, or if HbA1c remains under 6.5% without any diabetes medications other than metformin. Metformin is excluded from this medication list because there is no reason to stop it in most people whose diabetes has been reversed. That's because it has been shown in humans to prevent progression from prediabetes to diabetes, and because it also has been shown in animals to extend life and health.

Can Type 2 Diabetes Be Reversed ?

All of this makes for a nice story, but up until recently it has been pretty much a hypothetical game of connecting dots. What's needed is the evidence that T2DM in humans can be prevented or reversed by withholding dietary carbohydrates to a level that allows nutritional ketosis to occur. Before insulin was discovered and purified in 1920, going back to the time of the Greeks, the only treatment for diabetes was total starvation or severe carbohydrate restriction, but there was no practical dietary strategy that made this a sustainable solution.

The turning point came in 1976, when Bistrian *et al* reported seven cases of type 2 diabetes reversal for one year using a very low calorie ketogenic diet[7]. Following that, there have been multiple attempts to confirm and extend this pioneering report[8,9,10,11], but all of these clinical studies have used a ketogenic diet for only a few months, followed by a return to diets rich in carbohydrates. Dashti *et al*[12] reported a series of 30 cases of T2DM reversed by a ketogenic diet over 56 weeks, but did not report how many patients were initially enrolled, and they did not report what, if any, medications were taken by these patients.

We have many anecdotes of people with T2DM who have utilised a long-term, well-formulated ketogenic diet to loose excess weight, but more importantly many of them also returned their blood glucose values into the normal range for years without medication[3]. While some would claim that this is merely an effect of weight loss per se, Boden *et al*[14] demonstrated dramatic improvements in both blood glucose control and insulin sensitivity in just two weeks when a ketogenic diet was eaten to satiety. This is consistent with the observations of Shimazu[4], Newman[5], and Youm[15] showing that modest blood levels of ketones directly regulate genes that protect us from oxidative stress, insulin resistance, and inflammation.

Which brings us back to the question: can type 2 diabetes be reversed? Given the recent discoveries that beta-hydroxybutyrate (ketone body) triggers dramatic reductions in oxidative stress and inflammation, which in turn reduce the root cause of insulin resistance, there is just one remaining question—can a well-formulated ketogenic diet be followed long term? If the answer to this question is yes, then it follows that type 2 diabetes definitely can be reversed.

Making diabetes biomarkers like HbA1c or fasting plasma glucose better for a few months or even a year is good. Doing it while reducing medication use and reducing excess weight is even better. But if these benefits cannot be sustained, it is just another rollercoaster ride that so many people with T2DM have previously experienced. The

key piece to this puzzle is sustainability.

Getting real people to substantially change what they eat and continue to do so for years is really hard. Most people with T2DM have been educated to increase their exercise, avoid dietary fats, eat "healthy carbs," and limit calories. Reversing this failed treatment paradigm takes targeted education and coaching, but this process is aided when it delivers positive and self-reinforcing results. Early and sustained success with improved blood glucose control, reduced medication use, and medically significant weight loss creates patient empowerment and positive outcomes.

How Low :

Inducing a state of nutritional ketosis and maintaining it long enough to complete keto adaption requires a conscientious effort to restrict carbohydrates for two or more weeks. The level of carbohydrate restriction required to optimize fat burning and fat loss varies from person to person, but the most consistent effects will be obtained at below 50 grams per day[16].

This is often asked: "Why to recommend starting at 30 grams?" After all, there is no actual physiological need for any amount of carbohydrate in the human diet. The answer is that 30 grams is a level that most people can consume and remain in nutritional ketosis, and at the same time affording us a wider range of food choices. Carbohydrates from nutrient-rich sources like non-starchy vegetables, nuts, seeds, and full fat dairy products provide enhanced variety, texture, and essential minerals like magnesium, potassium, and calcium. This 30 g requirement will change over time based every individual's unique biochemistry and level of carbohydrate tolerance. Most people fall b/w 30-50 grams of required carbohydrates to stay in optimal nutritional ketosis (b/w 1-3 mmol blood ketones).

How Fast to Cut Back ?

The answer is not clearly spelled out by objective research as one would like. Some authorities advocate easing into carbohydrate restriction slowly by cutting back one food category at a time (eg, first sugars and juices, then refined carbs, then starchy vegetables, etc). Others take the "Nike approach" – as in "just do it". To date, no one has done a study with a large group of subjects to see which strategy yields a higher proportion making an effective transition into nutritional ketosis.

What we do know is that it takes a couple of weeks to keto-adapt, and you don't accomplish much towards that goal until you are making substantial amounts of ketones (ie, eating less than 50 grams of carbohydrates for most people). The other concern with easing into a low carb diet is that once you are eating less than the 150 grams of carbohydrates needed to feed brain with glucose, but still more than the 50 grams threshold below which ketosis is dependably operating, the brain's fuel supply becomes pretty tenuous. If there's not enough glucose to meet the brain's 600 calorie daily energy habit, and blood ketones remain below the 0.5 millimolar threshold where they can begin to pitch in, the body's only two options are:

(1) Burn up protein (for gluconeogenesis to fill the gap) or

(2) Binge on carbohydrates

In our clinical experience, the "Nike" approach is better. Particularly, if enough sodium is consumed and plenty of low carbohydrate vegetables eaten to get enough potassium, your adaption period will be short and relatively symptom-free.

Conflict of Interest :

Authors are associated with Novique Health Pvt Ltd., a start-up working in field of diabetes reversal using very low carbohydrate diet approach and providing continuous remote diabetes care.

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