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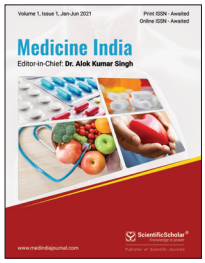

Editorial

Revert diabetes

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INTRODUCTION

One of the things that needs to be realized is type 2 diabetes mellitus (Type 2 DM) is an entirely reversible entity. And one thing that needs to be understood is that this is not a disease that will progress. Still, we often tell people that it is a chronic progressive disease. Even the American Diabetes Association or the diabetes Australia says that this is a chronic progressive disease. They tell people that if we have diabetes, we will have it for the rest of our life, and we all as well get used to those sayings, but the problem is that it is not true. It is straightforward to prove it. Type 2 DM is a disease of excess sugar, and it is a dietary disease.

Type 2 diabetes mellitus (Type 2 DM) is a reversible entity, but we should know how to reverse it. We will get worse if we do not know how to reverse it. In Type 2 DM, there will be high blood sugar because of too much insulin resistance, but that is the symptom; the disease is too much resistance to insulin. Hence, all the treatments that we are giving are targeted at blood sugar which does not make any sense because it is almost like to give an example that if we have an infection over the leg, we need to treat that infection, so what is causing infection was bacteria. Hence, we need to give antibiotics, and at the same time, that infection might cause fever. Still, that fever is not the disease; the leg wound will worsen if we start treating that fever as if it is the disease because we ignore the disease and treat its symptoms. That is what we have been doing with Type 2 DM all these years; we are treating the blood sugar. Type 2 DM is not a blood sugar disease; it is a disease of excessive insulin resistance. Hence, if we are not treating the disease, the disease tends to progress, and that is what happens with Type 2 DM all these years.

Getting blood sugar to come down by losing weight, doing exercise, and cutting out all the carbohydrates which reverse the insulin resistance is far different and better than making blood sugar come down by force of medication and ignoring the actual disease. We have made this fundamental mistake over the past 20–40 years. Type 1 diabetes patients have too little insulin, so we should give them insulin. In contrast, Type 2 DM is a condition of excess insulin, we need to decrease insulin, but on the contrary, we are giving more and more insulin to a disease with too much insulin.

DISCUSSION

Is Type 2 DM a reversible condition?

We are trained that this is a chronic and progressive condition all these years. However, we have a glance over specific examples, and we can say that this is not true.

Example 1

Bariatric operation is also known as weight decreasing surgery or stapling of the stomach. In this surgery, part of the stomach is taken out and is cut into the volume of a walnut, so the patient cannot consume much. Because the patient is not taking much food, he will lose weight. But what happens to diabetes?

Lets have a glance at a clinical study here. In 2012, a trial study called Surgical treatment and medications potentially eradicate diabetes efficiently (STAMPEDE)[1] compared the results of gastric bypass operation with aggressive medical treatment (drugs) on obese Type 2 diabetics with excessive blood sugar levels. In this study, people are randomized into two sets. One set of people continued to stay on their medications and got the finest medical therapy. The other set got a weight-loss operation done. There is no change in the number of drugs people took while doing the finest medical treatment available in this trial. They keep taking the same number of medications. However, weight loss operation set, very rapidly; within months, they are coming off all their drugs. By 12 months, many of these people came off all their medications, and their blood sugars became utterly ordinary. Hence, it seems like diabetes is a reversible condition, and more than that, it is reversible very rapidly. Moreover, even other types of weight-loss operations, like gastric banding, have similar benefits. Gastric banding is a method where a belt is kept inside the stomach and tightened, so that patient cannot consume. Moreover, again, what we can observe here is that diabetes is getting reversed very rapidly. Hence, this is not a chronic and progressive disease; this is a reversible condition. I am not saying that gastric banding or weight-loss operation is the solution for all patients. Still, it simply states that the situation is exceptional, and that this is a reversible condition.

Example 2

Fasting seems to reverse diabetes. Nearly a 100 years ago, Dr. Elliott Joslin, the most renowned expert in diabetes, wrote this in the Canadian medical journal... "That temporary period of under-nutrition is helpful in the treatment of diabetes will probably be acknowledged by all after these 2 years of experience with fasting." Indeed, there were minor problems in his findings; at that time, he did not distinguish between Type 1 and Type 2 diabetes. It is very advantageous for Type 2 diabetes patients, and it does not impact Type 1 patients significantly. A few years afterward, with the discovery of insulin, all the focus shifted to insulin, and we all forgot about the dietary therapies.

Example 3

In recent times, Dr. Taylor of Newcastle University, United Kingdom, performed a "The counterpoint study"[2] and established recovery of pancreatic function with an ultra-low caloric diet. In this study, the blood sugar HbA1c levels decreased from 9.6 to 5.9 in 7 days.

Hence, in reality there are some therapies which can cure and there are some therapies which cannot cure. the therapies which can cure are – bariatric operation, fasting, and very little-crb diets, and the therapies that cannot cure are – insulin, other medicines, and a diet with low fat. Indeed, we can never presume which path all our current treatment strategies are heading. They all are heading in the direction of no cure. Moreover, that is the rationale for why we say – it is a chronic and progressive condition. However, it is not, as Type 2 DM is a curable and reversible condition. Medicines cannot make well a dietary disease. The cure should be a diet that must be the proper diet.

What is the way to think about Type 2 diabetes?

Type 2 DM is a disease of high insulin resistance, but it has two phases.

The Whitehall study – they observed the blood glucose levels in the years before the diagnosis of diabetes and concluded that by the point, we diagnose Type 2 diabetes, the patient had it for an extended period.[3] Blood glucose levels increase even up to 12–15 years ahead of the diagnosis. As glucose levels start to go up, the pancreas begins to generate more insulin, which keeps the blood glucose levels pretty stable. Hence, the fasting HbA1c remains < six, even 2 years before the diagnosis. Moreover, then, at a point in time, the pancreas that is compensating for the overproduction of insulin eventually reaches its limit and starts to shut down because it cannot cope with the high levels of insulin resistance. Hence, as it shuts down, then the blood glucose starts going up.

We all believe that elevated blood sugar destroys the pancreas; however, this is not true since blood glucose levels do not rise until after the pancreatic has failed. Before the pancreatic breakdown, the blood glucose level was pretty okay.

As we go from obesity to pre-diabetes and diabetes, our insulin resistance increases as measured by fasting insulin levels. Hence, the first phase, where we go from 15 to 2 years before the diagnosis of diabetes, insulin resistance increases, which is offset by hyperinsulinemia. After that, when one becomes obese and pre-diabetic, the insulin levels become above our blood glucose because it brings our blood glucose levels down. However, insulin production peaks and then declines over time.[4] Hence, it barely takes 1 or 2 years before a full-blown diagnosis of Type 2 DM for this compensatory mechanism of hyperinsulinemia for getting abortive. Moreover, the breakdown of the pancreatic beta-cell leads to elevated blood glucose levels, which is the second phase of the disease as the pancreas is no longer providing the compensation.

We have been taught that this is due to a kind of burnout called pancreatic burnout, where the pancreas fails. That is probably incorrect because Type 1 DM used to be as high as 95% in pediatric clinics, but now, it is 50–50; 50% of the patients in pediatric clinics are Type 2 DM nowadays. It is tough to state that the pancreas got burnt out in these 10–12-year-old children with Type 2, like nothing on their body, has burned out. It meant surely that the concept of pancreatic burnout was wrong. Moreover, that is what we should appreciate. What is causing the pancreatic beta-cell stoppage?

What about insulin resistance?

A signal for our body to stock up on food energy is insulin. We know in physiology that if we consume food, we increase insulin. Hence, as we eat, the insulin rises. Our bodies store dietary energy by converting it to glycogen in the liver or converting it to fat (*de novo* lipogenesis), which we keep as body fat.

When we do not eat, insulin levels come down, which is the signal that starts drawing back out the stored food energy. As a result, we break down the glycogen, and subsequently, we will break down fat cells, which is known as lipolysis.

All this is a natural cycle. As we have stored energy, we do not pass away in sleep every night, and we need not continue pumping food in always. Hence, insulin does two things: It transports glucose into the cell, which is a well-known function, and it also switches on *de novo* lipogenesis. Hence, we are going to stock up on energy as our insulin increases.

This is similar to the locking key system that we are talking about. Here, insulin acts as a key, and it opens the insulin receptor, the lock, and glucose can go into the cell.

Because people with Type 1 diabetes lack insulin, glucose cannot enter their bodies, and their bodies devastate regardless of what they eat. That is known as internal starvation.

If we glimpse Type 2 diabetics, there is nothing wrong with that lock and key; their insulin and insulin receptors are normal. However, because of some cause, the key cannot fit in the lock, perhaps there is a bit of an obstacle inside the lock, and it is blocking it up, leading to internal starvation as there is no glucose inside there. To overcome that resistance, the body then produces more insulin. Moreover, that is controversial here; if there was internal starvation, there should be no drive for fat storage and new fat production. However, as we know, Type 2 diabetics will have severe visceral adiposity, significant fatty liver, and all their organs swim around in the fat, which does not look like internal starvation because of how fat can be produced from the glucose when there is no glucose available in the cell. It resembles trying to construct a home with no bricks. Hence, this is the fundamental paradox of the locking key system, and we will be destined to fail as long as we contemplate the locking key mechanism.

We argue that the patient is adamantly opposed to glucose entering the cells, but we all know that in Type 2 diabetes, *de novo* lipogenesis is rampant. In the liver, there will be a lot of fat everywhere, and we know that VLDL and triglyceride levels will be excessive. Hence, the patient is not dead set against insulin; this insulin function is way more expressed.

We have got incorrect thinking about Type 2 diabetes all these years. When we consider the locking key mechanism and how we may state the same cell, same insulin receptor, and similar insulin levels that the liver sees, one outcome is becoming rebellious, while the other is becoming highly receptive.

Consider the liver similar to a balloon, for instance. If you have extra insulin all the time, which keeps on pushing all the sugar into the liver, ultimately, the liver gets full, which causes insulin resistance. Simultaneously, the liver begins to decompress by turning all of the excess glucose into fat (DNL) and sending it out. When DNL overcomes the export power of the liver, fat starts accumulating in the liver, causing fatty liver and leading to central obesity. Excess sugar and insulin over too long a period causes fatty liver.[5] Since if you have a large fatty liver, even if your insulin levels are high, you cannot just force it in because it is tougher. Insulin resistance rises with liver fat.[6] In Type 2 diabetic patients, a close association exists between the liver fat content and insulin dosage required, reflecting high insulin resistance.[7] All of this clarifies the core paradox of insulin resistance. It is not at all defiant; it just got overfilled.

That is why one of insulin's mechanisms is clogged while another is over accelerated. Moreover, we have seen that fatty liver is usually present before diagnosing Type 2 diabetes. Just consider the liver cells, the hepatocyte, as baggage. It is easy to place all that glucose inside the cell if it is vacant. However, once it is full, it is challenging to keep pouring glucose in. Pushing that glucose into the cell will demand more and more energy. There is nothing wrong with the baggage or clothes. The problem is, it just got full.

What we need to do now is drain that overflowing cell. It is not a case of internal starving; it is a case of overflow. It is a vicious cycle; excess glucose causes elevated insulin, leading to fatty liver and insulin resistance, which contributes to hyperinsulinemia.

Nowadays, we understand that the goal is not to use more antibiotics but to use fewer antibiotics. However, everyone's first reaction is to offer more and more. Similarly, fatty liver is a reversible condition, as hyperinsulinemia is a drive for DNL, the principal determinant of fatty liver disease; we can reverse the fatty liver by normalizing insulin levels. Furthermore, extra fat with moderate carbohydrate

consumption does not much modify hepatic fat synthesis, although high carbohydrate intake can raise DNL tenfold.[8]

What about pancreatic burnout?

There will be no chance for reversal if the beta cell is burned out. This is what we as physicians get taught all these years. However, If we do a bariatric operation, the weight comes down, and the number of diabetic medications also goes down radically. Gastric banding also shows the same effect. Hence, it indicates that there is a sizeable reversible component to it, although we have all been taught that it is not reversible.

Dr. Roy Taylor of the United Kingdom has done a lot of research on this. He identified that when we get to extremely low-calorie diets,[9] we may decrease pancreatic fat content or triglyceride content. As a result, it may take a little longer, but we can see a steady decline in the pancreatic fat and the pancreatic beta-cell function re-establishment by 2–8 weeks.

Moreover, what we have to identify here is that pancreas has not burned out; it just got bunged with fat and triglycerides. Dysfunction of the pancreas is all related to fatty infiltration. Phase 2 is the pancreas' fatty infiltration, which leads to beta-cell burnout. Type 2 diabetes is linked to a fatty pancreas.[10] Patients with Type 2 diabetes have more pancreatic and hepatic fat than non-diabetics.[11] The less insulin the pancreas produces, the more fat it stores.[12] That is the underlying pathophysiology of that.

What kind of medicines do we need to take to reverse diabetes?

Never think about what kind of drugs to be taken to revert diabetes. Instead, we have a glance at the cause of diabetes, and then we can simply reverse it.

Consider our bodies as a large sugar bowl; as we consume food, the sugar bowl gets filled and spills out into the blood. We usually take insulin; it takes the sugar from our blood and reintroduces it into our bodies. However, that sugar bowl is still full. When we keep pushing it in, we reach a point where eventually, we cannot push hard enough. Then, we raise the insulin dose, which helps for a while, but the problem persists. If we have the wrong answer, there is no point in how hard we work on that answer.

All of that extra sugar keeps finding its way into our bodies, and over time, our whole bodies begin to decay. Hence, if we have the wrong model, if our considerations are improper, then everything that happens is false.

Type 2 diabetes is an overflow model; so much glucose is inside the cell and so much glucose is outside because it cannot get in. Giving more insulin is an incorrect thing to do in this scenario. We should drain the entire thing out, and we should make that sugar bowl vacant. That is the only key, and that is how we can reverse diabetes. Consider how misunderstanding the insulin resistance paradigm has resulted in decades of erroneous treatments.

The ACCORD study,[13,14] the VADT study,[15] the ADVANCE study, the ORIGIN study,[16] and the TECO study all show a similar thing; intensive pharmacological therapy to lower blood glucose does not function. The ADVANCE study[17] was also identical.

Hence, if we want to reverse Type 2 diabetes, we must first recognize the correct paradigm. It is an overflow paradigm, not a broken-down locking key concept. If the issue is an excess of sugar in the body, the cure is simple. The first approach is to avoid adding extra carbohydrates, a low-carbohydrate diet. Moreover, the second thing to do is burn it off.

How to manage skinny type 2 diabetics?

The key is not the overall fat in skinny Type 2 diabetics. Internal fat, or ectopic fat, is the key, which is the discrepancy between diabetes and no diabetes.

Many persons with Type 2 diabetes are of normal weight, as measured by BMI. Those people have an excess of liver and pancreatic fat. They are also managed in the same way; make them decrease their carbohydrates. Skinny Type 2 diabetes is most commonly seen in Asians. When it comes to BMI and diabetes, Caucasians have a BMI of around 27, whereas Asians have a BMI of about 23.7 when they get diabetes.

Author's Contributions

1. Dr. Jonnalagadda Vihari:
   Concepts, Design, Data analysis, Manuscript editing and review, Manuscript preparation.
2. Dr. Neerukonda Sriteja:
   Data acquisition.
3. Dr. Samir Sahu:
   Definition of intellectual content.
4. Dr. Chandan Das:
   Definition of intellectual content.
5. Dr. Aswini Kumar Sahoo:
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10. Dr. Roja Thammineni:
    Experimental studies, Clinical studies.

CONCLUSION

The point to be noted is can we heal Type 2 DM? Moreover, the solution is yes; as long as we properly know what Type 2 DM is, the accurate paradigm of insulin resistance and beta-cell failure is yes. Moreover, the main thing is that we will not have all the complications like heart attacks, strokes, nephropathy, and neuropathy if we do not have diabetes.

Moreover, we all can achieve it without any drugs, operations, or prices. This is free intervention, and it is all about having the proper understanding and the correct information.

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