

An Adjunct Treatment Reverses Insulin-dependent (Type 1) Diabetes in a Teenager

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Abstract: Globally, more than 30 million people suffer from diabetes mellitus type 1 (T1DM) characterized by pancreas producing little or no insulin hormone to facilitate glucose entering cells for energy production. T1DM patients tend to suffer a higher overall rate of atherosclerosis, cancer, and end-stage renal failure. No drug or surgical therapy seems to halt its annual upward trend amongst children and young adults. Consequently, a significant number of sufferers turn to complementary or alternative therapies for help to arrest this chronic endocrine condition. This paper discusses how a well-designed evidence-based dietary and nutritional therapy with some lifestyle modifications might offer a solution for this highly complex autoimmune disorder. The treatment outcome demonstrated a partial regeneration of pancreatic islet beta cells with substantial improvement for all relevant serum and urine markers tested.

Keywords: Type 1 diabetes mellitus, insulin-dependent diabetes, juvenile diabetes, autoimmune disorder, nutritional therapy.

CASE PRESENTATION

Lee J., a slim 24-year old weighting 56kg, worked as an assistant chef at a restaurant serving local delicacies for a small town population in Peninsular Malaysia. He was on insulin injection for the past fifteen years after being diagnosed as suffering from *juvenile diabetes* (diabetes mellitus type I or T1DM) when he was eight years' old. After been advised by his regular physician to reduce intake of refined starch and sugar during his initial years of administering his daily insulin, he felt that he was not gaining any weight like the rest of his school friends. Concerned about being laughed at as a 'weakling', he decided to resume his favourite noodles, buns, bread, biscuits, titbits, and sweet tropical fruits. He received no serious objections from his prescribing physician after raising this dietary issue with him. Worried about him developing early heart disease or hyperuricemia (elevated blood uric acid levels), his parents had discouraged him from consuming eggs, nuts, seeds, and beans. Over the past decade, the patient noticed that the amount of insulin prescribed for daily injection was raised on several occasions after tests confirmed his serum glucose gradual elevation. Being an insulin-dependent diabetic condition, he was instructed not to leave home without his insulin needle for which his parents paid. Having heard about complementary treatment for diabetes from a relative, he called on DSY Wellness Center to seek advice on how he could organise his diets while minimizing the use of insulin which often

caused him to suffer from problems associated with hypoglycaemia (low blood glucose).

After reviewing his past and present medical records, the patient was advised to gradually make these dietary modifications with the objective of establishing a regular meal pattern with fairly consistent day-to-day caloric and carbohydrate intake:

- (1) Reducing substantially the regular intake of refined starches and sugars which require excessive insulin to process. Insulin is secreted primarily in response to blood glucose although dietary fats and protein augment this glucose-induced secretion [1]. Instead, most daily calories intake would come from complex carbohydrates such as leafy vegetables, yam, bamboo shoots, lentils, beans, seeds, and nuts. Dietary fiber intake tends to be consistently low and well below the recommended 30 gram /day in most diabetic patients [2-4]. Except for those prone to allergies, health concerns over bean/nut consumption may be unfounded since hyperuricemia is more likely to be induced by the widely available sweet tropical fruits high in fructose [5] for which the patient had several servings daily. Furthermore, beans and nuts are rich in magnesium which levels are often low in youngsters with T1DM [6] due to increased urinary excretion of this mineral despite good glycemic control [7].
- (2) Keeping fat intake to less than 30 per cent of total calories to avoid gaining further adipose (fat) tissues during therapy period [8].

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- (3) Reducing intake of trans fatty acids since these man-made fats promote insulin disorders and various other metabolic health problems [9].
- (4) Including yellow, green or black tea as beverage. *Camellia sinensis* (tea) beverages may mildly suppress appetite while reducing glucose and triglycerides by more than 20% [10].
- (5) Adding *Momordica charantia* L. (cucurbitaceae) to daily vegetable juicing or soup. This bitter-tasting melon could lower fasting glucose and improve glucose tolerance [11] by increasing glucose uptake [12] in the presence of some insulin [13]. Just 2 grams/day of the unripe melon has hypoglycaemic effect [14, 15] with higher dosages comparable to some prescription drugs for treating diabetes [16], but with no nephrotoxicity (kidney damage) or hepatotoxicity (liver damage) [17]. Its antidiabetic compounds include charantin, vicine and polypeptide-p [18], which can lower insulin need even on a high fat diet [19]. Improving *glycemic* control can improve markers of oxidative stress too [20, 21].
- (6) Juicing organic and freshly-harvested low-fructose local fruits such as *Garcinia mangostana* (mangosteen), *Mangifera indica* (mango) and *Psidium guajava* (guava). Mangosteen juice may be able to lower blood inflammatory marker C-reactive protein scores after just two months' therapy [22]. Freshly harvested unripe mango can also lower blood glucose [23]. Non-GMO (genetically modified organism) guava possesses strong free radical scavenging [24] as well as anti-inflammatory and antiglycative properties [25]. Both its hydrophilic and lipophilic antioxidant activities [26] seem to be contributed by its high ascorbic acid (vitamin C) content [27].
- (7) Serving generous amount of spices. *Trigonella foenum-graecum* L. (fenugreek) contains *emblica officinalis*, which can lower fasting blood sugar and glycated hemoglobin (HbA1c) levels in diabetes. *Cinnamomum Zeylanicum* (cinnamon) is a commonly used spice [28] which appears to mimic the effect of insulin. Indeed, many of T1DM patients are aware of the positive effect of cinnamon on their blood glucose levels [29]. It has hypoglycemic effects [30] which can significantly lower HbA1c score, which is a strong measure of diabetic control [31]. Furthermore, compounds such as the micro-mineral chromium and polyphenols found in cinnamon could improve patient's insulin sensitivity [32].
- (8) Adding cooked non-GMO *Triticum aestivum* (wheat) sprout to salad or vegetable dishes. Its polysaccharides may stimulate insulin production by pancreatic beta-cells and pancreatic islets [33].
- The patient was also advised to initiate these lifestyle modifications with immediate effect:
- (i) Exercising to improve muscle tone and/or help build a higher muscle mass, which could enhance his body's sensitivity to insulin [34]. Pancreas of a physically active or fit individual tends to secrete less insulin after being served carbohydrates than do physically unfit individuals [35].
- (ii) Avoiding 'diet' or 'light' cola or soft drinks since these beverages could make greater demand for insulin [36].
- Ceasing to cook protein food with sugary items under high temperatures. Formation in this manner of Advanced Glycated End-products (AGEs) in food could further damage his insulin-secreting beta cells. AGEs are accelerated in diabetes or during hyperglycaemic conditions, but their production also occurs in settings characterized by oxidative stress and chronic inflammation [37].
- When the patient's first set of blood and urine test results returned, he was advised to continue his insulin injection or any medication unless his regular physician ordered otherwise. As adjunct therapy, the following nutrients were prescribed to be taken after meals with the reasons explained to him:
- (1) ***Gymnema sylvestre extract***: 500 mg three times a day (TID). This herb helps stimulate insulin release from beta cells [38] besides increasing efficiency of this hormone [39]. It also may help regenerate these insulin-producing beta cells [40, 41], lower HbA1c scores and increase C-peptide levels in T1DM patients [42].
- (2) ***Multivitamins and minerals***: once a day. Some 40% of patients on complementary therapy take a good combination of multivitamins /minerals [28]. Compared to non-diabetics, diabetics tend

to excrete significantly more minerals including zinc [43] needed for insulin production.

- (3) **Chromium polynicotinate:** 200mcg TID. This micromineral can help correct negative chromium balance common in youngsters with T1DM [44]. Being an essential nutrient involved in the metabolism of glucose and insulin, it can reverse glucose intolerance and neuropathy in T1DM [45] although dosages lower than 200mcg/day are unlikely to be effective [46].
- (4) **Alpha lipoic acid (ALA):** 200mg TID. Being an essential cofactor for mitochondrial bioenergetic enzymes, this nutrient improves glycemic control, prevents diabetic neuropathy [47, 48], treats different forms of autonomic diabetic neuropathy [49], improves microcirculation [50], and ameliorates pathophysiologies of many chronic diseases [51]. Elevated HbA1c raises risk of diabetic retinopathy, which is found in up to 60% of T1DM patients aged 20 and above [52]. Diabetes is associated with elevated oxidative stress including DNA-damaging hydroxyl radical formation [53].
- (5) **Vitamin A:** 10,000 IU twice a day (BID). This fat-soluble vitamin has immuno-modulatory effects, which are relatively deficient in subjects with established T1DM [54]. Consequently, diets rich in polyphenols and/or vitamin A have protective effects against autoimmune inflammatory attack of the islet beta cells and they have the potential to reduce the pathogenesis of autoimmune diabetes [55, 56].
- (6) **Mixed tocopherols:** 400 IU BID. Vitamin E ameliorates oxidative stress in T1DM and improves antioxidant defence system [57]. Even a modest supplementation can lower HbA1c and triglyceride levels in T1DM patients [58]. Free radical mediated oxidative stress can play a major role in the pathogenesis of diabetes. The glycation of proteins and elevated serum triglyceride levels are two of the major risk factors in the development of complications of diabetes. Vitamin E helps protect residual beta cell function of the pancreas [59].
- (7) **Ascorbic acid:** 1g TID. Chronic hyperglycemia in T1DM patients induces permanent alterations of their endothelial function by increased oxidative stress, even after glycemia is normalized. As a strong antioxidant, vitamin C can normalize endothelial function in these patients [60] and slow progression in hypertension and/or heart disease. It reduces sorbitol accumulation in erythrocytes promoted by hyperglycemia [61] by inhibiting the enzyme erythrocyte aldose reductase [62].
- (8) **Folate:** 800mcg BID. Endothelial dysfunction, a precursor of vascular disease, begins early in T1DM and is associated with low folate status with high-dose folate normalizing endothelial dysfunction [63, 64], although it does not seem to do so in non-diabetics even if obese [65].
- (9) **Nicotinamide:** 500mg TID. This non-flushing vitamin B3 inhibits poly (ADP-ribose) polymerase, reduces nitric oxide accumulation in pancreas, and can protect beta cells against radical-induced necrosis [66]. It can preserve baseline C-peptide secretion [67], which augments blood flow in skeletal muscle and skin, diminishes glomerular hyperfiltration, reduces urinary albumin excretion, and improves nerve function in patients with T1DM [68]. Just 25mg/kg of body weight seems effective in reducing insulin-producing beta-cell dysfunction [69].
- (10) **Vitamin D3:** 4000 IU TID. Of the various environmental causes, this anti-autoimmune vitamin is rather well-studied in relation to T1DM [70-74]. Patients may achieve lower HbA1c levels if they have higher serum 25-hydroxyvitamin D levels [75], although some studies showed only a small positive effect on fasting glucose [76].
- (11) **Magnesium citrate (elemental value 16%):** 1g TID. One in four diabetic patients [77] may suffer from hypomagnesemia, which can lead to poor diabetic control with higher HbA1c scores [78], early atherosclerosis [79] and microalbuminuria [80]. Its deficiency can cause retinopathy and hypertension [81], metabolic syndrome [82], and chronic diabetic complications [83] since it is a co-factor in more than 300 different enzyme systems in the body [84]. Insulin injection can enhance renal magnesium excretion [85]. Supplementation can improve insulin sensitivity and may stimulate insulin secretion [86].

DISCUSSION

T1DM is characterized by the infiltration of activated T-lymphocytes and monocytes into the islets of

Langerhans of the pancreas, resulting in chronic inflammation and progressive destruction of the insulin-producing beta cells [87, 88]. Activated T-cells and cytokines secreted from immunocytes act synergistically to destroy these beta cells resulting in the development of this autoimmune disease [89]. Once islet auto-antibodies have developed, the progression to diabetes in antibody-positive individuals is determined by the age of antibody appearance and by the magnitude of the autoimmunity [90]. Globally, some 33 million people suffer from T1DM and its incidence increases by about 3% annually among children [91]. T1DM patients appear to face a higher overall incidence of cancer [92] and end-stage renal failure [93].

Vitamin D receptor (VDR) gene polymorphisms may determine risk of developing T1DM with the environment influencing the association between VDR genotype and T1DM risks [72]. The disorder commonly begins during childhood but may appear later in adulthood in a proportion of 30 to 40% of affected individuals [94].

Parent's eating habits and the home food environment such as its accessibility and availability are important determinant of their children's dietary intake [95, 96]. The likelihood of children making positive changes to their diets will be increased if their parents are involved and supportive. Vegetables and low-fructose citric fruits consumption should be raised [97], while long-chain saturated fats intake should be lowered [98, 99] since atherosclerosis may be well-established when T1DM children reach adolescence [100, 101].

Increased intake of omega-3 fatty acids and fish oil is linked to reduced T1DM-associated autoantibody conversion [102]. Use of cod liver oil rich in vitamins A and D in the first year of life is associated with a significantly lower risk of T1DM [103]. Vitamin D3 supplementation in early childhood can offer protection against the development of T1DM [73, 104] as well as helping to reverse its increasing incidence [105].

A long list of environmental factors influences the risks for or progression to T1DM [87], which condition is on the rise globally [106] and especially in children [107]. The presence of multiple autoantibodies seems to have the highest positive predictive value for development of T1DM [108, 109]. Insulin autoantibodies, in contrast to the other autoimmune markers, are the only beta-cell specific antibodies [110].

There may be a link between viral infections and the first appearance or increase in islet antibodies [111-113] although the evidence is weak [114, 115]. However, viral infection of antigen presenting cells can locally raise inflammation and auto-reactive lymphocytes [116].

An early onset of T1DM can raise the child's risk of learning disability [117]. Difficulties in diagnosing T1DM are a significant cause of diabetic ketoacidosis development in children with new-onset disease [118].

A cure for T1DM may require the provision or elicitation of new pancreatic islet beta cells as well as the reestablishment of immunological tolerance [119]. The limited regenerative ability of the endocrine pancreas may be linked to the defined number of pancreatic progenitors, which is generally incapable of compensatory growth in response to cell loss [120]. The inability to cure this chronic disorder is largely because of its highly complex pathophysiology [121].

Some 28% of the population in developed nations depends on complementary and alternatives modalities to treat their T1DM [28] although there seems to be insufficient research evidence to support differing nutritional needs for those with T1DM compared to type 2 diabetes [122].

The Diagnosis

The patient suffered from most of the major symptoms of juvenile diabetes such as polyuria (frequent urination), polydipsia (increased thirst), polyphagia (increased hunger), and weight loss [123]. His dramatically reduced HbA1c score after three months' therapy suggested a much lower level of glycated hemoglobin and a stronger diabetic control. Such a score could also be linked to his lower triglyceride levels [99]. The fasting insulin and glucose levels in November 2013 would suggest his pancreatic islet beta cells were releasing adequate insulin to meet his needs after some dietary modifications. This supports long-held belief that there would still be some functional beta cells in people with longstanding T1DM [124]. His chronic inflammatory conditions improved five-fold accompanied by much lower level urine microalbumin. The patient was delighted with the disappearance of any glucose from his urine sample taken at the end of the third month of therapy. This positive outcome was confirmed by the patient's regular physician, who then advised a temporary halt to the administration of insulin pending further monitoring.

Extracts from the patient's three months' test results for 2013 were as follow:

| | Aug | Sept | Oct | Nov |
|---|------|------|-----|-----|
| <u>Serum</u> | | | | |
| Fasting insulin (2-25uU/ml) # | <2 | <2 | 5 | 16 |
| Fasting glucose (<115mg/dl) | 253 | 218 | 167 | 104 |
| HbA1c (<5%) | 8.3 | 7.2 | 6.4 | 5.9 |
| hs-CRP (<1.0mg/L) | 15.9 | 11.7 | 7.3 | 2.8 |
| Fibrinogen (2-4g/dl) | 5.3 | 4.5 | 3.9 | 3.1 |
| Triglycerides (<150mg/dL) | 312 | 287 | 242 | 159 |
| # Morning scores without insulin injection for 12 hours | | | | |
| <u>Urine</u> | | | | |
| Glucose (nil) | **** | ** | * | nil |
| Microalbumin (<3.4mg/mmol) | 23.2 | 16.7 | 9.5 | 4.2 |

Although cytokines such as IL-1alpha, IL-1beta and IFN-gamma are widely implicated in the pathogenesis of autoimmune diabetes [125], local laboratories were unable to test these markers.

The patient was using the insulin pump and with flexible injection regimens designed for him to lead a normal lifestyle [126]. However, initial test results suggested his inability to benefit fully from these modern conventional therapies.

CONCLUSION

The health outcome achieved by the patient suggested some form of pancreatic cell mass regeneration consequent upon undertaking this nutritional therapy which involved some lifestyle modifications. Further study involving a higher number of patients with similar conditions is warranted to elucidate its wider therapeutic benefits in the treatment of T1DM.

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