

A Functional Medicine Protocol for Diabetic Foot Ulcers: A Case Report

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Abstract

Diabetes is still in the top 10 causes of death worldwide. In 2012, diabetes mellitus produced 1.5 millions of death related to different complications that included lower limbs amputation. This is a case of a 59-year-old Hispanic man with diabetes mellitus type 2 (DM2). The patient arrived with a diabetic foot ulcer in the pad of the left foot. The patient's ulcer began to heal after being treated with high doses of intravenous (IV) vitamin C, a metabolic correction protocol, that included a paleolithic diet, supplements to: high potency multivitamin, B complex, Vitamin D, Omega-3, Coenzyme Q10, Acetyl-L-Carnitine, alpha lipoic acid, magnesium, mixed phospholipids and combination formulas GlucoCoR® and Circulat® (supplements for sugar metabolism improvement). The treatment for diabetes was changed to Lantus, Humulin, and Enalapril. He was also given hyperbaric oxygen therapy (HBOT) three times a week. According to the results obtained in this clinical case, we advise extending the study of the function of Vitamin C combined with a metabolic correction oral protocol, a paleolithic diet, and HBOT as a potentially effective treatment in patients suffering from advanced diabetic foot ulcers.

Introduction

Recent data from the World Health Organization has projected that diabetes will be the seventh leading cause of death in 2030. This is due to the increasing prevalence of people around 18 years old with the disease which has increased from 4.7% to 8.5% in the past three decades globally [1]. Moreover, the number of adults living with diabetes has quadrupled since 1980 from 108 million to 422 million in 2014 due to factors such as overweight and obesity. In 2012 DM caused 1.5 million deaths from complications that lead to heart attacks, stroke, blindness, renal failure and lower limb amputation [1]. According to Bourne et al. [2], 2.6% of global blindness is attributed to diabetic retinopathy, and the disease is among the leading causes of kidney failure [3].

Diabetes mellitus is defined as a metabolic disorder identified by the presence of chronic hyperglycemia and also accompanied by deterioration in the metabolism of carbohydrates, lipids, and proteins [4]. Based on the American Diabetes Association most people living with diabetes fall into the categories, (a) diabetes type 1 (DM1) or (b) diabetes type 2 (DM2) [5]. Diabetes mellitus type 1 is commonly caused by an autoimmune destruction of beta cells of the pancreas hindering its ability to produce insulin [4] although in some patients the cause is idiopathic [6]. According to Mahler and Adler, diabetes mellitus type 2 presents with peripheral insulin resistance, defective regulation of hepatic glucose production and also a reduction in beta cell function [7].

The clinical complications of DM2 include macrovascular and microvascular diseases [8]. Microvascular complications include retinopathies, nephropathies, and neuropathies, and macrovascular complications are coronary heart disease and peripheral vascular disease [9]. Diabetic peripheral neuropathy (DPN) boosts the risk of foot injuries, secondary infections, ulceration and amputations [10]. According to Al-Rubeaan et al. [11], the risk of ulceration and amputation increase with progression of age and duration of diabetes by fourfold. The diabetes foot ulcers are characterized by a skin breakdown on foot in diabetic patients [12], and more frequently occurs in the forefoot, with the same incidence on the plantar and dorsal surface [13]. DPN is caused by several pathways: (1) increased formation of advanced glycation end products (AGEs) [6]; (2) over activation of polyol pathway which produces increased amounts of sorbitol and depletes NAD(P)H and inhibits the production of (ROS) scavengers, like glutathione [6]; (3) the Protein Kinase C dependent activation of NAD(P)H Oxidase [6], which damages tissues by excessively increasing the amounts of Reactive Oxygen Species (ROS), increases vasoconstriction and reduces the blood flow directed to the nerves [10]; and (4) raised hexosamine pathway, where fructose-6-phosphate is converted to uridine diphosphate-N-acetylglucosamine, which indirectly increases microvascular damage [6].

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Diabetic foot ulcers are slow or non-healing lesions that form on feet of diabetic patients and increase the risk of lower-limb amputation [1,14]. 60% of non-traumatic lower-limb amputations are performed in people with diabetes. As reported in 2010, around 73,000 non-traumatic lower-limb amputations are performed in adults with diabetes annually [15].

Although amputation is advised when infection threatens the overall health of the patient, this course of action has a negative effect on mobility and lifestyle of the patients. Diabetics with these complications have a poor quality of life and are more likely to have a higher risk of premature death [1].

Xie et al. [15] mention that diabetic foot ulcer patients, who have a higher prevalence of infections and vascular complications, more frequently experience malnutrition in comparison with diabetics without foot ulcers. According to Gonzalez et al. [16], to function normally the body needs over 40 vitamins and micronutrients, fats (omega-3,6,9), proteins (8 essential amino acids), carbohydrates (complex), nutrient factors: coenzyme Q10, acetyl L-carnitine and lipoic acid. The metabolic correction regimen has the primary goal to enhance health by optimizing enzyme efficiency [17] employing micronutrient combinations [18]. Devitt et al. [19] allude that epidemiological observation have shown that improving glycemic control lowers the risk of developing macrovascular and microvascular complications. In Masharani et al. [20] study, it was found that in the diabetic type two patients placed on the Paleolithic diet show a more significant improvement in glucose control and lipids profiles in comparison with a conventional diet based on moderate salt intake, low-fat dairy, whole grains and legumes.

Several studies have confirmed that the body needs certain elements to produce the necessary energy to stay healthy and fight diseases. Metabolic correction implies a series of changes in a person's diet with a low glycemic load, increased hydration patterns and micronutrient supplementation that enhances the metabolism and mitochondrial energy production while addressing the biochemical root of the disease [10]. Moreover, it provides the biochemical explanation on how the use of nutrients can work with therapeutic and preventive purposes against disease [16].

Vitamin C and glucose are very similar in structure so they compete for the same transport system. Previously published data show improvement in glycemic control with vitamin C supplementation [21,22]. IV vitamin C is a more concentrated way of providing this essential nutrient.

The emergence of hyperbaric oxygen therapy (HBOT) as an adjunct to therapy of diabetic foot lesions has its basis in the fact that it can reduce anaerobic infection, improve circulation (blood supply) and decrease ischaemic damage to nerves [23].

In the search of an affordable effective treatment mechanism that lowers the risk of developing diabetic complications, this case reports the adoption of an unconventional treatment based on a metabolic correction therapy in the case of a diabetic foot ulcer, resulting in complete healing of the wound and regaining neural sensation and saving of the affected limb.

Case Report

This is a case report of a 59-years old Hispanic man who arrived with a painful grade 3, stage C, foot ulcer in the pad of the left foot. He was diagnosed with Diabetes mellitus type 2 in March 2000 and treated with Metformin 500 mg twice a day.

Before starting the treatment blood tests of the patient showed HA1C of 9.0%, T4 levels of 0.59 ng/dL, CBC showed RBC 4.38 m/UL, HGB 13.0, RDW-CV of 16.7%. The comprehensive metabolic panel showed glucose of 227 mg/dL, BUN 35 mg/dL and potassium 6.1 mmol/dL. The lipid panel showed cholesterol of 203 mg/dL and triglycerides of 276 mg/dL.

The patient was placed on a Paleolithic diet consisting of roots, wild caught fish and shellfish, lean organic grass fed meat, organic eggs, fruits, vegetables and nuts and treated with high doses of IV vitamin C. He was first treated with a regimen of vitamin C 25 g tiw



Figure 1: Progression of the patient diabetic plantar foot ulcer recovery (The ulcer classification was made using the University of Texas wound classification)

for a week, after that 50 g tiw for a week. A third therapeutic sequence of 75 g tiw was given, all this for a period of three months. The patient was also treated with supplements po: B complex sublingual (1 cc) bid; a high potency multivitamin and mineral was provided qn; Omega- 3's (1 g) were given tid, Coenzyme Q10 (100 mg) tid, Acetyl-L-carnitine (250 mg) bid, Alpha- Lipoic Acid (300 mg) tid, Magnesium citrate 500 mg tid Vitamin E (200 mg) tid, Vitamin D 10,000 IU qn, Mixed phospholipids 100 mg qn. GlucoCor® (supplement for sugar metabolism improvement, MetaCor, LLC) 3 caps tid. Circulat® (botanical Supplement for glycemic control, Medicina Sistemica, LLC) 5 capsules bid.

The treatment for his condition of diabetes was changed to Lantus and Humulin 70/30 Pen and was also prescribed and Enalapril 20 mg. The patient was also given hyperbaric oxygen therapy (1.5 ATM for 45 min, biw) (Figure 1).

Discussion

According to Guo and DiPietro the vitamins C, A, and E are potent antioxidants and have anti-inflammatory properties [24]. Vitamin C has a significant role in wound repair and healing regeneration [25] because it is used as a cofactor in two of the enzymes of the procollagen biosynthesis. Different studies have found that diabetes increases the amount of ROS [26]. Dakhale et al. [27] mention that Ascorbic Acid is an antioxidant vitamin that has a molecular structure similar to glucose and can supersede these monosaccharides in many chemical reactions which is why it's so effective in avoiding non-enzymatic glycosylation. It reduces blood glucose, improves glycosylated hemoglobin, and it also protects against ROS damage.

Two important risk factors for developing diabetic foot ulcers are peripheral neuropathy and sensory loss [28]. The Alpha lipoic acid can regenerate other antioxidants such as Vitamin C, Vitamin E, and glutathione, and could be used as an alternative treatment for chronic disease related to oxidative stress [9]. Studies conducted in diabetic type 2 patients using oral antioxidant thioctic acid (alpha lipoic acid)

found an improvement in neuropathy symptoms [29,30], another study that used intravenous administration of 600 mg of alpha lipoic acid for three weeks also reported a reduction in neuropathic pain [31]. Sima et al. [32] published the results of a clinical study showing that acetyl L-carnitine improved symptoms in patients with diabetic neuropathy. Also, a metabolic corrector supplement has been shown to improve glucose parameters in type 2 diabetics [33].

Glycemic control is a critical aspect of the management of diabetes. As mentioned previously, in a Masharani et al. [14] study it was found that diabetic patients placed on the Paleolithic diet show a more significant improvement in glucose levels in comparison with a standard diet based on nutrition recommendations of the American Diabetes Association. Jonsson et al. [34] found that the Paleolithic diet was more satiating per calorie in comparison with diabetic diet. In a study conducted by Whalen et al. [35], it was found that Paleolithic or Mediterranean diets could be associated with lower levels of systemic inflammation and oxidative stress.

Metabolic correction therapy consists of providing the body with micronutrients (vitamins and minerals in their active forms) that are required for health [16]. Metabolic correction is considered to be reached when the body succeeds in achieving optimal levels of nutrients. At this stage, the cells and enzymes have replenished their co-factor quota needed to correct biochemical disruptions produced by nutrient deficiency or insufficiencies [17]. At a biochemical level, this homeostatic (balanced) state induces an overall metabolic and physiologic improvement in which the body has enough nutrients and energy to heal itself [36].

GlucocoR® was incorporated to the therapeutic protocol for blood glucose level control. As part of this therapy, it acts as a metabolic corrector by improving enzyme function. It was formulated to maintain normal blood glucose levels, decrease homocysteine levels, protect against oxidative damage and promote healthy tissues and collagen formation. The formula consists of Alpha lipoic acid, Acetyl L carnitine, Chromium, Vanadium, B-Complex, Magnesium, Zinc and Green tea extract (in their most active forms).

Circulat® was also included as part of this protocol to further enhance balancing glucose and inflammation parameters. It consists of a combination of 22 synergistic herbs formulated to maintain normal blood glucose levels, improve circulation and protect against oxidative damage. The formula consists of *Angelica Sinensis*, *Crataegus oxyacantha*, *Equinacea angustifolia*, *Equinacea purpurea*, *Croton lechieri*, *Electrococo senticosus*, *Ganoderma lucidum*, *Ginkgo biloba*, *Grifola frondosa*, *Hydrastis canadensis*, *Centella asiatica*, *Rhaponticum carthamoides*, *Panax ginseng*, *Panax quinquefolius*, *Petiveria alliancea*, *Pfaffia paniculata*, *Rhodiola rosea*, *Ruscus aculeatus*, *Sutherlandia frutescens*, *Tabebuia avellanaeda*, *Uncaria tomentosa* and *Vaccinium myrtillus*.

Vitamin C can enter cells through glucose transporters [37]. It can be taken into the cell in the place of glucose, decreasing its intracellular levels and, thus, helping lower glucose-induced damage. Vitamin C can also enter the mitochondria and protect the membrane from ROS [38], and improve mitochondrial energy metabolism [39]. It could also have an ergogenic capacity by donating electrons to the electron transport chain resulting in increased energy production [40]. It is also essential for the synthesis and maintenance of collagen, necessary for connective tissue formation [40]. Consequently, Vitamin C should be considered as a treatment for slow healing foot ulcers [40,41].

Hyperbaric oxygen therapy (HBOT) increases the oxygen that is delivered to tissues. Given that diabetic foot ulcers are associated with ischemia, this therapy has been used to increase wound healing [42]. Studies have demonstrated that HBOT is an effective adjunctive treatment to enhance foot ulcer healing and reduce limb amputation in diabetic patients [43,44].

Conclusion

We suggest further studies using a combination protocol of Paleo diet, high dose IV Vitamin C, metabolic correction

therapy, phytomedicinals and hyperbaric oxygen as therapeutic tools for Diabetes, especially advanced diabetic foot cases.

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