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Metabolic Correction As a Proposed Approach for Reduction of Complications and Costs of Diabetes Care in Puerto Rico

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Abstract

Diabetes is among the leading causes of death and disability worldwide. In the United States, diabetes is a principal cause of kidney failure, non-traumatic lower-extremity amputations, and blindness among adults. In Puerto Rico, given the even higher prevalence of this condition than in most countries, implementation of innovative, science-based and cost effective strategies is urgent. Despite the implementation of accepted treatment guidelines that include diet and medications, the prevalence of the disease, its complications and costs continue to rise. In this concept paper, costs estimate of diabetes and its complications in Puerto Rico are presented and discussed. A brief discussion of the limitations of current treatment guidelines and how metabolic correction may help overcome some of those limitations are included. Finally, we briefly discuss how the implementation of metabolic correction may reduce the costs of diabetes and its complications.

Keywords

Diabetes, Metabolic Correction, Diabetes Cost

Diabetes Background and Statistics

Diabetes Mellitus (DM), a metabolic disease characterized by glucose and insulin abnormalities, often leads to many complications such as heart disease, stroke, hypertension, blindness, kidney disease, nerve disease and many others. This condition is among the leading causes of death and disability worldwide [1]. In the United States, diabetes is a principal cause of kidney failure, non-traumatic lower-extremity amputations, and blindness among adults [2]. In the US population the prevalence of DM is 8.3% (2011) and ranks as the 7th cause of death [3]. Globally, it has been estimated that 366 million people had diabetes, 50% of them undiagnosed in 2011 with estimated projections of 552 million people with diabetes by the year 2030 [4]. In Puerto Rico, the scenario related to DM is much worse, having a prevalence of 12.9% (approximately 500,000 persons) for 2009 and reaching the 3rd cause of death [5-10].

The Cost of Diabetes

The social cost of Diabetes Mellitus (DM) in the USA for 2012 was \$245 billion (\$176 billion in direct medical cost and \$69 billion in loss of productivity) [11]. Of that cost, \$47 billion are for chronic diabetes-related complications [11,12]. Complications of Diabetic Peripheral Neuropathy (DPN) as it continues its natural course, produces increasing pain, loss of sensation, ulcers, infections, amputations and death. In addition to suffering, disability and loss of productivity, there is a very significant economic impact related to the treatment of DPN and its complications. In USA alone, it has been estimated that more than 5,000,000 patients suffer from DPN, and the total annual cost of treating the disease and its complications is over \$10 billion [13]. There is another concern with people that do not yet meet the diagnostic criteria of diabetes, but have blood glucose in the upper level of normal values. It has been shown that these people have increased risk of other diseases (such as cancer, nerve, kidney, cardiovascular and others) [14-17]. It has been estimated that the cost of pre-diabetes for the 57 million adult population in 2007 in the USA exceeded \$ 25 billion [10,18].

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With respect to Puerto Rico, there is no published or official estimate of the social cost of DM. However, in an unpublished report submitted by Dr Marín to the Center of Diabetes of Puerto Rico in 2012, the annual social cost of DM for the adult population was estimated to be \$2,290 million [19]. Out of this, \$1,559 million (68%) were in direct costs to the healthcare system and \$731 million (32%) were for indirect costs due to productivity loss. From the direct costs, 56.9% was generated by patients older than 64, and for indirect costs, 89% was generated by patients younger than 65. The per capita (per person) annual social cost of DM patients was estimated in \$6,351, distributed in \$4,324 for direct costs and \$2,027 for indirect costs. Per capita annual costs among the older patients (over 64 years old) were \$6,825; for middle age (45 to 64) were \$6,124, and for younger patients (18 to 44) were \$5,800 [18].

Diabetes medical costs are expected to maintain a constant growth during the next years. Evidence to this fact is the trend demonstrated by a recent market study that shows diabetes care sales having a Compound Annual Growth Rate (CAGR) higher than that of the general pharmaceutical industry sales. The study estimated that while the total pharmaceutical prescription sales (are) expected to have a growth rate 3.6% CAGR by the year 2015, diabetes care will experience a CAGR of 7.8% for the same period [20]. Recently, Standard & Poor's estimated that the annual market for diabetes drugs will hit \$58 billion by 2018, from about \$35 billion today (2013)[20] whereas a *Transparency Market Research* study estimated the market for diabetes drugs and devices to attain a size of \$114.3 billion by 2016, following a growth rate of 18.2% [21]. (Table 1)

The World Health Organization latest published numbers on diabetes prevalence showed that diabetes is a growing global problem, with high and increasing costs to society and the individual [22]. Mayor pharmaceutical companies are incurring in substantial capital investment responding to what they have recognized as the growing diabetes epidemic. Keeping the diabetes care cost low is of great concern, especially since 80% of people with diabetes live in low to middle-income countries [22,23].

Diabetes Clinical Data (Limitations of Clinical Treatment Guidelines)

Current Clinical Management Guidelines of DPN are based on adequate glucose control and symptomatic pain relief [24]. Careful glycemic control could delay the onset or slow the progression of diabetic neuropathy in patients with diabetes mellitus, but it does not completely prevent the progression of the disease [15]. Elevated glucose levels are a fundamental biochemical abnormality, but not the only metabolic abnormality implicated in the DM pathophysiology.

In order to be able to reduce complications of DPN, it is crucial

to improve or correct the metabolic conditions that lead to the pathology present in this condition. The first step toward this end must be an appropriate diet that will foster insulin sensitivity, reduction of blood glucose and glycation and reduction of inflammation. In order to accomplish this, carbohydrates must be well controlled in balance with healthy sources of proteins and fats. These are necessary macro- changes. However, micro-changes are often needed for the fine tuning of metabolism and achieving healthy state. These changes are key to further improve metabolism. Proper diet is the fundamental basis of health, providing a balance of macro and micronutrients. The metabolic needs of any particular person are a balance of the combination of external factors (contaminants, microorganisms and other stressors) and the body's own internal factors (genetically determined individual metabolic capacity). In certain circumstances, diet alone might not be enough to account for these unmet metabolic needs, and allow re-establishing a healthy physiology. An innovative, scientific-based approach aimed to correct the biochemical abnormalities of the disease denominated "Metabolic Correction" has been proposed.²⁵⁻³⁰ The main objective of this publication is to present Metabolic Correction as a cost effective therapy to complement current therapeutic methods.

Metabolic Correction As a Therapeutic Tool for Diabetes

Metabolic correction is the utilization of a synergistic combination of micronutrients and cofactors in the active forms and doses that maximize the function of metabolic enzymes in most individuals. Metabolic correction helps improve or rectify biochemical disruptions associated with a diversity of dysfunctional mechanisms that lead to degenerative states. Metabolic correction is the fine tuning of the cellular biochemistry by means of specific nutritional supplementation with the goal of improving cellular, tissue, organ, system and organism function [29].

Pathophysiologic mechanisms implicated in diabetic neuropathy include: increased polyol pathway with accumulation of sorbitol and reduced Na⁺/K⁺ATPase activity, microvascular damage and hypoxia due to nitric oxide deficit and increased oxygen free radical activity. Moreover, there is a decrease in glutathione and the increase in homocysteine. Clinical trials in the last two decades have demonstrated that the use of specific nutrient cofactors can correct some of these metabolic derangements, improving symptom control and providing further benefits such as improved sensorium, blood flow and nerve regeneration. There is substantial evidence on those nutrient cofactors such as lipoic acid, acetyl-L-carnitine, benfotiamine and the combination of active B vitamins, L-methylfolate, methylcobalamin and pyridoxal-6-phosphate, providing important

| Age Groups | Adult patients ² (18 or older) | | Direct costs to the healthcare system (ambulatory, inpatient, medications, laboratories, etc...) | | Indirect costs (loss of labor productivity) | | Total costs | |
|-------------|---|--------|--|--------|---|--------|------------------|--------|
| | n | % col. | \$ | % col. | \$ | % col. | \$ | % col. |
| 18 to 45 | 54,361 | 15.1% | \$ 133,249,124 | 8.5% | \$ 182,064,683 | 24.9% | \$ 315,313,806 | 13.8% |
| 46 to 64 | 164,444 | 45.6% | \$ 539,206,934 | 34.6% | \$ 467,782,023 | 64.0% | \$ 1,006,988,957 | 44.0% |
| 65 or older | 141,878 | 39.3% | \$ 887,048,763 | 56.9% | \$ 81,289,899 | 11.1% | \$ 968,338,661 | 42.3% |
| Total | 360,684 | 100.0% | \$ 1,559,504,821 | 100.0% | \$ 731,136,605 | 100.0% | \$ 2,290,641,425 | 100.0% |

Table 1: Estimates of Social Costs of Diabetes in Puerto Rico for the year 2010¹

1. Dr. Heriberto Marin used estimates for the social costs of Diabetes in the United States as based to generate estimates for Puerto Rico. The source used for the US was the following: *United States Economic Cost of Diabetes in the U.S. in 2007*, American Diabetes Association, Diabetes Care, Volume 31, Number 3, March 2008. In order to generate the estimates for Puerto Rico the following steps were taken: 1) the number of adult diabetic patients in Puerto Rico by age group was obtained from the BRFSS, 2) the average direct and indirect cost by patient were imputed from the US, 3) costs were aggregated for each age group to generate total costs, 4) figures were inflated to the year 2010 using the price indexes for Puerto Rico, and 5) all figures were adjusted downward using the fact that Medicare payments in Puerto Rico are in average 60% of those in the US.
2. According to the Behavioral Risk Factor Surveillance System (BRFSS) for 2010. <http://www.cdc.gov/brfss/>

benefits for patients with diabetic neuropathy [31-36]. Metformin, the first line drug in the management of diabetes type 2, uses folic acid and B12 for its metabolism, therefore people with poor nutrient intake, gastrointestinal malabsorption and metabolic susceptibilities may be at risk of drug-induced nutrient depletion when using this form of therapy [37,38]. In addition, there is a high prevalence of the polymorphic gene mutation of MTFHR in the Hispanic population [39,40]. This could pose a significant risk for depletion of the active form of folic acid, as well as an increase in homocysteine both linked to an increased risk of developing DPN.

Health and Economic Projections of the Utilization of Metabolic Correction As a Therapeutic Tool for Diabetes

The health benefits of metabolic correction can be divided into its impact in the complications of the condition and in the reduction of adverse drug events. One such complication is the elevated risk of cardiovascular diseases observed in diabetes patients. Therefore safer diabetes treatment needs to be sought. Recognizing this need, the US Food and Drug Administration published guidelines for the industry requesting that entities with drugs under review or to be developed for treatment of diabetes prove that such drugs do not increase adverse events of cardiovascular outcomes [41].

The integration of Metabolic Correction in the management of people with medical conditions such as diabetes or at risk for serious complications such as DPN, constitutes a new paradigm. Considering the whole cost of the management of the pre-diabetic and diabetics including the cost of medications, the management of the adverse effects of medications and the cost of complications; the use of metabolic correction is expected to improve outcomes beyond current accepted guidelines and reduce overall cost. Considering the published literature [\[42\]](#) concerning the effect of individual nutrients on diabetic peripheral neuropathy, a synergistic formulation based on the concept of metabolic correction would be expected to result in improved outcomes. The evidence in published reports pertaining to the reduction of the complications of DM amounts to 10-20% when integrated as part of a judicious treatment [31-36]. A metabolic correction formula is expected to improve glucose levels as well as other biochemical parameters providing better blood supply, improving nitric oxide status, reducing homocysteine and improving cellular aerobic energy. Overall, this is expected to result in reduced morbidity and mortality, improved quality of life and increased productivity in the affected population.

Cost of Medication related morbidity and mortality (MM) in ambulatory patients in the USA has increased more than two-fold from \$76 billion/yr in 1995 to \$177 billion/yr in 2001 [42,43]. At this rate of increase, the Cost of Medication related MM should surpass \$700 billion by 2013 [44]. There are no estimates of Cost of Medication related MM for Puerto Rico, but adjusting for the differential in payment in costs between USA and PR it could be estimated between \$2,000-\$4,000 million.

Scholars in pharmaco-economics have proposed the concept of Pharmaceutical Care (PC) as a way to improve health care and reduce cost [45,46]. Despite the importance of PC, its ability to decrease costs has a limit in the vicinity of 20-30%. Its limitations are related to its inability to prevent the progress of the disease and the effect of medication-induced nutrient depletion. Interestingly enough, there are indications that intensive lifestyle interventions can prevent or delay the onset of diabetes related complications in people with diabetes [46]. We propose Metabolic Correction as a complementary concept to PC to produce further improvements in both clinical outcomes and cost reductions related to medication MM. This concept has cost savings implications not only in the creation of public policies, but for the individual decisions. Patients have to pay medical visits, once their health insurance exceeds the of a visit and treatment. For some patients this may have significant economic costs since they have to pay full for their follow up treatment.

Conclusion

Given the amount spent in Puerto Rico for the complications of DM (\$304 million), the use of this innovative strategy (Metabolic Correction), is expected to produce savings of \$30-60 million of dollars. In addition, further benefits could be expected when factoring the effect of Metabolic Correction on the cost of Medication-related MM (adverse effects). If the cost of the adverse effects is between \$2 to 4 billion, then the potential savings from metabolic correction for this would be \$300-600 millions. Therefore, the net savings from the use of metabolic correction is very significant because it reduces both the complications and cost of the disease and the adverse effects of the medication. The impact of Metabolic Correction of reducing adverse effects, complications and cost saving potential can be tested in various models. We have proposed and will proceed testing a simple model of Metabolic Correction in diabetic patients with modification of the type of macronutrients and proportions, hydration and supplementation (Table 1).

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