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Clinical Parameters of Metabolic Control (HbA_{1c}) and Deterioration of Peripheral Arterial Perfusion in Type 2 Diabetes

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Abstract

Objective: To determine the relationship between clinical parameters (HbA_{1c}) whit metabolic control and deterioration of peripheral arterial perfusion in diabetic patients. **Methodology:** 108 medical records of patients with type 2 diabetes mellitus were evaluated. We obtained averages of: blood glucose (162.3 ± 73.10 mg/dl), glycated hemoglobin (HbA_{1c} = 7.64% ± 1.77%), cholesterol (189.28 ± 35.25 mg/dl), triglycerides (189.11 ± 87.76 mg/dl), Systolic Blood Pressure (SBP = 119.69 ± 14.95 mmHg), Diastolic Blood Pressure (DBP = 77.15 ± 9.55 mmHg) and Media Blood Pressure (MBP = 91.36 ± 9.89 mmHg). We correlated variable HbA_{1c} with vascular injury symptomatology. **Results:** Correlation was found between sensitivity dysfunction and HbA_{1c} with a statistical significance of p = 0.01, and a correlation Kendal coefficient w = 0.01, any other parameter of metabolic control was not correlated with symptoms of vascular injury. **Conclusion:** It is remarkable that the sensitivity dysfunction is a symptom of poorly vascularized lower extremities caused for both functional impairment and structural changes in diabetic patients' peripheral nerves, even in the preclinical stage of vascular disease. The HbA_{1c} could also be investigated as a likely sensitivity dysfunction biomarker in DM due to the correlation presented in this study but more studies must be realized.

Keywords

Protein Glycation, Vascular Disease, HbA_{1c}, Type 2 Diabetes Mellitus

1. Introduction

Diabetes mellitus (DM) remains a major health care problem worldwide due to associated complications and prevalence both in developing and developed

countries [1]. The people with it face an array of health issues such as: 1) It is the leading cause of lower-limb amputation non-traumatic, new cases of blindness, and kidney failure complications that affect the daily activity; 2) It is also a major contributor to cardiovascular disease, the number one cause of death in world. It is predicted that within 15 years (2030), there will be 500 million people worldwide with diabetes if we do not take the necessary measures to prevent the spread of this serious and costly disease.

The medical costs for treating patients with DM represent an important spending, the projections for 2020 close to 200 billion USD, or even higher. It also causes loss of productivity resulting in spend for the patient and his family [2]. In Mexico, the National Institute of Public Health (2010), ranked the DM as third cause of disability in men and the fifth in the women [3], 80% of the disabilities in diabetics are caused for vascular complications could be averted through adequate prevention and early intervention. The strategies are focused on prevention and intensive treatment and are cost-effective when the first focus on people at high risk of developing the disease and second in hypertension control, cholesterol and glucose levels among diagnosed people [4] [5].

In the past two decades, they have accumulated considerable evidence that supporting the potentially pathogenic role of some number of mechanisms that lead to the development of vascular complications mainly the diabetic foot among which are: nerve ischemia, oxidative stress, glycosylation and products and other molecular disorders. These changes cause damage to nerve fibers and lead to the development of peripheral vascular disease where endothelial dysfunction is the most serious result as it affects limb microcirculation [6].

The chronic hyperglycemia in diabetic patients leads to changes at biomolecular, anatomical and physiologic level. These changes induce the development of vascular complications such as the peripheral arterial disease (PAD) and thus to poorly vascularized extremities whit considerable risk for amputation contribute to diminished quality of life and even death of diabetics [7].

Advanced glycation end products (AGEs) contribute to a variety of microvascular and macrovascular injuries mostly leads to Peripheral Vascular Disease (PVD) cause of blindness, chronic renal failure and nontraumatic lower-limb amputation in diabetic patient in Mexico [8] [9]. The National Nutrition Health Survey in 2012 [5] founded 38% (2.4 millions) of patients with a previous DM diagnosis reported the presence of burning, pain or loss of sensation in the feet. Besides, also reported a prevalence of amputations or 2% (182 thousand people) and the latter were associated with an evolution of the disease of approximately 12 years [6] [10]. Nontraumatic lower-limb amputation is usually preceded by a foot ulcer in 85% of patients, and cases so that the association between ulcers and lower limb amputations is obvious, it is also known that patients require subsequent amputation and that the greater part of the amputated, there are higher risk of death within 5 years [11].

In general terms, Treatment of Peripheral Vascular Disease (PVD), like other complications of DM, should focus first on metabolic control and then the spe-

cific actions, that is, emphasize early detection risk factors such as: hyperglycemia, dyslipidemia, hypertension, etc. [8]. In some contexts of health, as in some Mexican provinces, is difficult to carry out good metabolic control in patients with DM as it has not reactive required for this, it is why it is necessary to have risk markers with high specificity and sensitivity in identifying PVD.

This study addresses the issue on the identification of risk markers to determine the peripheral vascular damage in patients with Type 2 DM, specifically HbA_{1c}, so as to enable health personnel identify potential damage service users and intervene in an effective and timely manner. 97% of hemoglobin corresponding to a molecular form represented as HbA1, 2.5% or less to HbA2 form and less than 1% to the HbF form the union of different sugars favors the formation of HbA_{1a}, HbA_{1b} y HbA_{1c}; the latter is the most abundant (approximately 80%) in the bloodstream. HbA_{1c} it has been used for over 10 years, to establish the diagnosis of DM in different populations, to determine the degree of metabolic control that the patient has had in the last three months and as a marker of coronary risk tissue [12]. The purpose of this study was to establish whether there a relationship between clinical parameters of metabolic control (blood pressure, plasma glucose, triglycerides and HbA_{1c}) with the deterioration of peripheral arterial perfusion in patients with a clinical diagnosis of type 2 DM current or later production of electronic products.

2. Materials and Methods

2.1. Study Design and Sample Size

This study was documentary quantitative and the study subjects were clinical records of patients with type 2 *Dibetes Mellitus* and deterioration of peripheral arterial perfusion symptoms (n = 108 records). The inclusion criteria were patients with type 2 DM records with follow-up consultation record (of one year); patients who have test HbA_{1c} results, blood glucose, cholesterol, triglycerides and that the clinical records mentions the presence of symptomatology of vascular dysfunction. The exclusion criteria were records of diabetic patients with any type of anemia, with renal failure and iron pharmacological therapy. These three conditions alter the results of glycosylated hemoglobin.

2.2. Data Collection

The parameters obtained were: HbA_{1c}, blood glucose, blood pressure (BP), Mean Arterial Pressure (MAP), cholesterol and triglycerides these values were related with skin disorders or signs and symptoms to deterioration of peripheral arterial perfusion.

2.3. Data Assessment

The clinical parameters were related with the percentages of symptoms related to vascular damage and overall error and standard deviation of each variable was calculated. The Pearson correlation coefficient (r=) Kendall coefficient, (w=) between HbA_{1c} and decreased peripheral pulses, paleness in lower limbs, delayed

capillary refill, changes in temperature, sensitivity dysfunction, alteration nail-beds, onychomycosis, venous insufficiency ulcers, hyperkeratosis were obtained.

2.4. Ethical Concerns of the Study

The development of this research was based on Article 17 of the General Health Law in research without risk [13]. The protocol included the authorization of general manager of Mexican Social Security Institute (Clinic 14, in March 7, 2016; number of trade Of. Dir. 084/16).

3. Results

The records were constituted for 82 women files and 26 men files (n = 108) in this study. In the clinical records the patients were 59.19 ± 13.86 years old and the predominant marital status was married with 76.9%, the single status was 0.9%. The year's evolution for the disease had an average of 9.12 ± 6.42 years (see Table 1).

The average of clinical disease evolution was 9.12 ± 6.42 years and the metabolic control parameters with 12 months of follow-up are on the Table 1, nevertheless, the greater data deviation was plasma glucose (>140 mg/dL), followed cholesterol (<160 mg/dl), see Table 2.

No results found of decreased peripheral pulses, delay in capillary refill, and changes in temperature or pain nevertheless, our results showed that paleness of the limbs had an average of 4.26% ± 0.79%, sensitivity dysfunction was 2.93% ±

Table 1. Socio-demographic data of patients with type 2 *diabetes mellitus* (n = 108).

Sex	Distribution of patients by sex			
	Frequency		Percentage	
Female	82		76%	
Male	26		24%	
Total	810		100%	
	Age of patients			
Minimum		Maximum	Average	Standard deviation
Age	35	95	59.19	13.86
Distribution of patients by marital status				
	Frequency		Percentage	
Married	83		76.9%	
Single	1		0.9%	
Widower	20		18.5%	
Free Union	4		3.7%	
Total	108		100%	
Years of evolution of Diabetes Mellitus in study subjects				
Minimum		Maximum	Average	Standard deviation
Years of progression disease	1	30	9.12	6.462

1.67%, presence of recorded edema was 4.5% ± 2.01%, alteration in nail beds found an average of 2.70% ± 1.25% among others parameters (see Table 3).

In relation with the correlation of variables, we found no statistical significance between most of them except as regards HbA_{1c} and the presence of altered sensitivity. Pearson correlation coefficient was r = −0.20, with a value p < 0.50. Regarding the correlation coefficient Kendall, it was w = 0.01, with a value p < 0.01, which is statistically significant (Figure 1).

Table 2. Average clinical parameters of metabolic control in patients with type 2 diabetes mellitus (n = 108).

	Glucose	HbA^{1}_{1c}	Cholesterol	Triglycerides	SBP^{2}	DBP^{3}	MBP^{4}
Average	162.36 md/dL	7.64%	189.11 md/mL	189.11 md/mL	119.69 mmHg	77.15 mmHg	91.36 mmHg
Standard deviation	73.10	1.17	35.25	87.76	14.95	1.43	9838
Standard error	7.03	0.17	3.39	8.44	9.55	0.91	0.95

Data represent $\dot{X}$ ± DE a monthly readings of a study records corresponding to patients with Type 2 DM. [1]Glycated hemoglobin fraction 1c, [2]Systolic Blood Pressure, [3]Diastolic Blood Pressure, [4]Media Blood Pressure.

Table 3. Average values of the different symptoms of vascular damage (n = 108).

Symptoms of vascular damage	Average (%)	Standard deviation (%)	Standard error (%)
Paleness of the lower extremity	4.26	0.79	0.07
Sensitivity dysfunction	2.93	1.67	0.16
Edema	4.5	2.01	0.19
Alteration nailbeds	2.70	1.25	0.11
Onychomycosis	39.59	8.57	0.82
Venous insufficiency	38.24	9.78	0.94
Ulcers	0.63	0.70	0.06
Hyperkeratosis	8.57	1.58	0.15

Data represent $\dot{X}$ ± DE a monthly readings of a study records corresponding to patients with Type 2 DM.

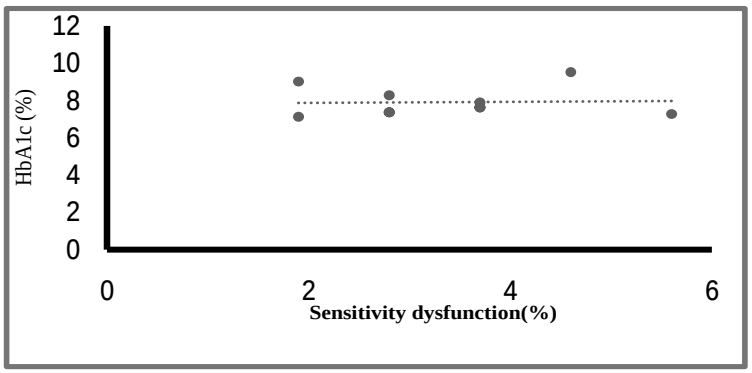

Figure 1. Correlation between HbA1c variable with the sensitivity dysfunction. (Data represent % of HbA_{1c} and % of sensitivity dysfunction an average of 12 months; n = 108; p < 0.01).

4. Discussion

Diabetes and its complications put a great economic burden on patients, their families, healthcare systems and countries [1]. A correlation was found between the awareness about the disease complications and mean self-care agency scores of the diabetic subjects. Those who were aware of disease complications had higher self-care agency scores than those who were unaware of them [14]. However, a study showed that there was no significant correlation between the presence of complications and self-care [15].

Our results show a clear metabolic breakdown in all patients throughout the study period since each parameter was found to be well above normal values [16]. In spite of the above, we did not find statistical relation of the registered parameters and symptomatology of vascular damage except between HbA_{1c} and sensitivity dysfunction, which is consistent with studies that have associated HbA_{1c} as a marker of risk with cardiovascular disease [17] [18] [19] [20] [21], mainly in coronary arteries, not in damage to other organs such as the kidney [22] or liver [23]. Ramesh and col (2015), evaluated the role of hepato-biliary function as a marker of predictor Coronary Artery Disease (CAD) in patient with Type 2 DM. 100 subjects included 50 T2DM patients with CAD and 50 T2DM without CAD were evaluated and their finding implies that decreased serum bilirubin increases the risk of CAD in patients with Type 2 DM and it shows inverse correlation between HbA_{1c} and bilirubin [24].

On the other hand, results found in our study regarding the symptomatology of sensitivity dysfunction differ from those reported by different authors [25] [26] [27], studies in which, claudication and pain are the most prevalent symptoms in the PVD during stadiums I and II. In the present study, the most prevalent symptom was the presence of onychomycosis followed by hyperkeratosis, probably due to changes in endothelial cell proliferation which compromise the activity of the immune system-inhibition of fibroblasts and damage to the basement membrane of keratinocytes [27]. Hyperkeratosis has been associated with collagen glycosylation in keratinocytes which results in thick skin, dry and rough in the lower limbs and its presence has been associated with ulcerations in the diabetic foot [28].

Presence of sensitivity dysfunction is the main symptom of diabetic polyneuropathy—loss of peripheral nerve fiber function—considered the most common predictor of diabetic foot ulceration and symptom associated with a lack of metabolic control of the patient [29]. This result indicates that HbA_{1c} could also be investigated as a likely marker of risk of diabetic neuropathy—Necessary condition for the appearance of ulcers in Type 2 DM patients. In other studies [30] [31] HbA_{1c} has shown its effectiveness both in the diagnosis of Type 2 DM, as well as cardiovascular risk, damage to the retina and diagnosis of DM. There are no other studies related to HbA_{1c} and sensitivity dysfunction in lower limbs.

5. Conclusions and Suggestions

- In this study, a correlation was established between HbA1c and sensitivity

dysfunction in lower limbs.

- The correlation found in this study is an important finding of clinical impact which would allow emphasizing the importance of metabolic control through the measurement of HbA1c in patients with Type 2 DM.

- The authors suggest that this positive correlation can be used as a likely marker of loss of sensitivity.

Conflict of Interests

The authors declare that they have no conflict of interests.

Authors' Contribution

This study was designed by Ma. de Lourdes Zúñiga-Martínez and Ángel Antonio Vértiz-Hernández. Patient selection and data collecting were organized and made by Yolanda Terán-Figueroa and Laura Escarlet Guerrero-Cruz Statistical analyses were done by Ángel Antonio Vértiz-Hernández, statistical expert. The paper was written by Ma. de Lourdes Zúñiga-Martínez, Yolanda Terán-Figueroa and Ángel Antonio Vértiz-Hernández.

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