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ORIGINAL

Factors that impact in the answer of the ulcers from the diabetic foot to the Heberprot-P®

Factores que inciden en la respuesta de las úlceras del pie diabético al Heberprot-P®

Sergio Alberto Díaz Cruz[1], Talia Batista Villar[1], Doraimys Valido-Valdes[1], Ymirsys Núñez Núñez[1], José Luis Fernández González[1]

[1]Universidad de Ciencias Médicas de Pinar del Río, Dirección Municipal de Salud, Consolación del Sur. Pinar del Río, Cuba.
[2]Universidad de Ciencias Médicas de Pinar del Río, Policlínico 1ro de Enero, Consolación del Sur. Pinar del Río, Cuba.

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Corresponding Author
Sergio Alberto Díaz Cruz

ABSTRACT

Introduction: the diabetes mellitus constitutes a problem of health to world scale for its growing incidence and for its complications, mainly associated to the vascular damage that you/they usually present, as the ulcer of diabetic foot that can take to the amputation and discapacidad.
Objective: to identify the factors that impact in the answer of the ulcers from the diabetic foot to the Heberprot-P® in patient belonging to the policlínico September 5, Consolation of the South, Pinegrove of the River, in the period of January 2022 and January of the 2024.
Method: he/she was carried out an observational, analytic, and traverse study. The universe was represented by all the diabetic patients (n=1875) belonging to the selected policlínico and the sample for those with ulcer of the diabetic foot, treaties with Heberprot-P®. (n=28). Theoretical, empiric and statistical methods were used.
Results: the patients prevailed with more than 70 years (64,2 %), feminine sex (65,3 %) and white color of the skin (71 %). The arterial hypertension (56,3 %) and the obesity (8,6 %) they are the observed pathological antecedents. The most frequent localization in the ulcers was the region metatarsiana (28,57 %), 60,7 % of these lesions healed before the 3 months. the time of cure of the lesion showed statistical relationship with the presence of obesity, tabaquismo and an inadequate feeding and the biggest age.
Conclusions: the age, obesity, the tabaquismo and the alimentary habits were factors that impacted in the answer of the ulcers from the diabetic foot to the Heberprot-P®.

Keywords: Diabetes Mellitus; Factors of Risk; Diabetic Foot; Heberprot-P®.

RESUMEN

Introducción: la diabetes mellitus constituye un problema de salud a escala mundial por su creciente incidencia y por sus complicaciones, principalmente asociadas al daño vascular que suelen presentarse, como la úlcera de pie diabético que puede llevar a la amputación y discapacidad.
Objetivo: identificar los factores que inciden en la respuesta de las úlceras del pie diabético al Heberprot-P® en pacientes pertenecientes al policlínico 5 de Septiembre, Consolación del Sur, Pinar del Río, en el período de enero 2022 y enero del 2024.
Método: se realizó un estudio observacional, analítico, y transversal. El universo estuvo representado por todos los pacientes diabéticos (n=1875) pertenecientes al policlínico seleccionado y la muestra por aquellos con úlcera del pie diabético, tratados con Heberprot-P®. (n=28). Se emplearon los métodos teóricos, empíricos y estadísticos.
Resultados: predominaron los pacientes con más de 70 años (64,2 %), sexo femenino (65,3 %) y color blanco de la piel (71 %). La hipertensión arterial (56,3 %) y la obesidad (8,6 %) son los antecedentes patológicos más observados. La localización más frecuente de las úlceras fue la región metatarsiana (28,57 %), el 60,7 % de estas lesiones sanaron antes de los 3 meses. el tiempo de curación de la lesión mostró relación estadística con la presencia de obesidad, tabaquismo y una alimentación inadecuada y la mayor edad.
Conclusiones: la edad, obesidad, el tabaquismo y los hábitos alimentarios fueron factores que incidieron en la respuesta de las úlceras del pie diabético al Heberprot-P®.

Palabras clave: Diabetes Mellitus; Factores de Riesgo; Pie Diabético; Heberprot-P®.

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INTRODUCTION

Chronic noncommunicable diseases (CNCDs) are a major public health problem worldwide.[1] They are the leading causes of morbidity and mortality among older adults in developed and developing countries, with hypertension and diabetes mellitus (DM) being the most common.[2,3]

DM is a syndrome of impaired carbohydrate, fat, and protein metabolism caused by a lack of insulin secretion or decreased tissue sensitivity to insulin.[4]

There are two general types of diabetes mellitus. Type 1 diabetes, also called insulin-dependent diabetes mellitus, is caused by a lack of insulin secretion, and type 2 diabetes, also called non-insulin-dependent diabetes mellitus, is initially due to a decrease in the sensitivity of target tissues to the metabolic effect of insulin. This reduced sensitivity to insulin is often referred to as insulin resistance.[4,5]

The International Diabetes Federation estimated a global prevalence of diabetes in adults aged 20-79 years in 2021 of 10,5 %, with an increase to 11,3 % by 2030 and up to 12,2 % by 2040.[6]

The incidence of diabetes is increasing rapidly, with estimates suggesting that this number will almost double by 2030. Diabetes mellitus occurs worldwide but is more common in developed countries. The greatest increase in prevalence in the near future is expected to occur in Asia, the Middle East, and Africa, where there is likely to be a 50 % increase in diabetes in these parts of the world by 2030.[7]

According to official data from 2018, the prevalence of type 2 DM in Mexico was 10,3 %. In addition to the above, it is estimated that the percentage of individuals with undiagnosed DM is just over 50 %, highlighting the need for timely diagnosis to enable adequate care to delay potential sequelae of the disease at the individual, family, and societal levels.[8]

The prevalence rate in Cuba in 2022 was 66,5 per 1 000 inhabitants, and in Pinar del Río, it was 68,5 per 1 000 inhabitants, making it the province with the sixth highest prevalence.[9]

This disease is considered a global health problem due to its increasing and high incidence and prevalence rates. At the same time, it is a major cause of morbidity and mortality in the adult population and a risk factor for the development of other vascular diseases, which are among the leading causes of death worldwide and in Cuba.[10]

Diabetic patients often have complications, which generally appear over the years, especially in patients without adequate metabolic control. Long-term complications are mainly vascular and varied and are due, at least in part, to chronically high blood glucose levels, which lead to damage to blood vessels.

Diabetic foot ulcers (DFUs) are one of the most feared complications of DM, leading to amputation and disability, social exclusion, and early mortality. It has been estimated that the lifetime incidence of foot ulcers reaches up to 34 % of individuals with diabetes, while diabetes-related lower limb complications affect approximately 159 million people worldwide. As a result, the diabetic population still accounts for 80 % of all non-traumatic lower limb amputations worldwide.[11]

According to the WHO, DPU is defined as infection, ulceration, and destruction of deep tissues of the lower extremity, associated with neurological alterations and varying degrees of peripheral vascular disease. Age, poor metabolic control, abnormal immune response, deformities, and the presence of vasculopathy and neuropathy are some of the risk factors closely related to its onset.[12]

DUP is a condition with an annual incidence of 2 % which, according to European studies, occurs in 19 to 34 % of patients with diabetes mellitus throughout their lives. In Latin America, it is the reason for hospitalization in 3,7 % of cases and in 20 % of patients hospitalized with diabetes mellitus.[13]

Depending on age, gender, and place of origin, the prevalence of diabetic foot ranges from 2,4 % to 5,6 %. The incidence of foot ulcers in these patients can reach 15 % of patients with diabetic foot. Up to 85 % of those who undergo amputations secondary to diabetic foot have previously suffered from a diabetic ulcer. In Argentina, 8 % of hospital beds are occupied by diabetic patients, usually with foot ulcers. Nineteen amputations are performed daily, approximately 7 000 per year, and 7 out of 10 are diabetic patients.[14]

It is estimated that 15 % of patients with diabetes will develop ulcers at some point in their lives. The treatment of diabetic foot is very expensive and takes a long time to heal. In Cuba, the Center for Genetic Engineering and Biotechnology (CIGB), an institution in the capital's scientific hub, has developed recombinant human epidermal growth factor through the drug Heberprot-P®, a unique product in the world that has changed surgical concepts related to diabetic foot ulcers and opened up a range of therapeutic possibilities for these patients, improving their quality of life. The drug is injected into the lesion. This drug has pharmacologically relevant properties, as it allows the establishment and consolidation of useful and productive granulation tissue in diabetic patients with healing difficulties. This includes de novo angiogenesis at the wound site; it also stimulates the secretory phase of granulation, particularly in patients with neuropathies, in whom granulation tissue is usually facelable, and wound contraction and remodeling.[15]

Treatment with Heberprot-P® in Cuba has marked a turning point, with very good results, including its inclusion in a national and international program for its implementation as an effective therapy to resolve this problem in a high percentage of patients affected by DPU.[16]

Heberprot-P® has accelerated ulcer healing, reducing the risk of amputation by 71 % in the Cuban population; it has been administered to more than 88 000 patients in 12 years; and has prevented some 17 000 amputations. Since 2007, when its application began in grade 3-4 ulcers, according to the Wagner International Classification, and in amputee patients, excellent results have been obtained, reducing the amputation rate and the average length of hospital stay. It is currently used in all polyclinics in Cuba and in 37 countries around the world.[15]

The Cuban health system develops strategies aimed at reducing disability in diabetic patients, thereby contributing to a better quality of life for patients and a greater contribution by them to society. It is therefore feasible to conduct studies to evaluate the

effectiveness of the different treatments applied and programs established to contribute to their improvement.

The objective of this article is to identify the factors that influence the response of diabetic foot ulcers to Heberprot-P® in patients at the September 5th polyclinic in the municipality of South Consolidation in the province of Pinar del Río, during the period from January 2022 to January 2024**.**

METHOD

An observational, analytical, and cross-sectional study was conducted.

Universe: the universe was represented by all diabetic patients (n=1875) belonging to the "September 5th " health area in the municipality of South Consolidation.

Sample: The sample was represented by all patients with diabetic foot ulcers treated with Heberprot-P® at the September 5th polyclinic in the municipality of South Consolidation (n=28).

Inclusion criteria

Patients with the characteristics described who agreed to participate in the study.

Exclusion criteria

Patients whose final treatment outcome is unknown.

To conduct the study, a survey was administered to collect information that met the research objectives, with the prior informed consent of the participants.

The information obtained from the municipal diabetic foot clinic registry was stored in a spreadsheet for analysis. Inferential statistics were used, and different statistical tests were applied: absolute and relative frequency; Mann Whitney U test (p); Pearson correlation.

RESULTS

Table 1. Patients with diabetic foot ulcers treated with Heberprot-P® according to age and sex

Age (years)	Sex					
	Female		Male		Total	
	No	%	No.	%	No.	%
Under 60	6	21,4	0	0	6	21,4
From 60 to 69	3	10,7	1	3	4	14,3
From 70 to 79	4	14,3	5	17,9	9	32,1
Over 80	5	17,9	4	14,3	9	32,1
Total	18	64,3	10	35,7	28	100,0

Table 1 shows that the sample is predominantly made up of patients over 70 years of age (64,2 %) and female (65,3 %).

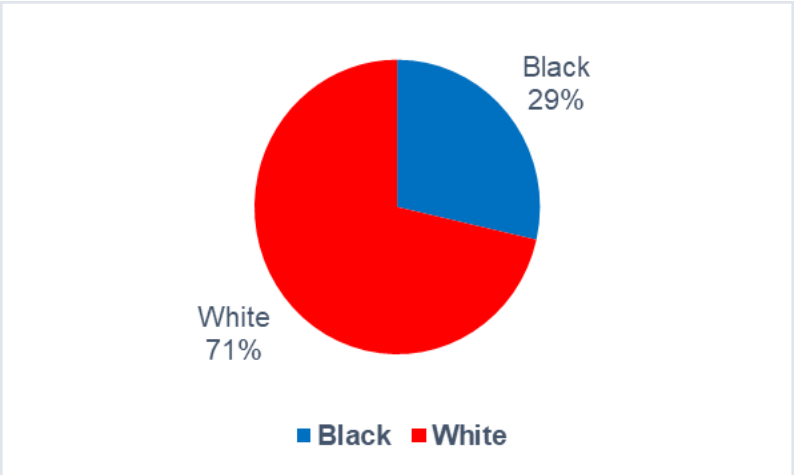


Figure 1. Patients with diabetic foot ulcers treated with Heberprot-P® according to skin color

Figure 1 shows that the predominant skin color is white, representing 71 % of the total number of patients.

Table 2. Personal medical history in patients with diabetic foot ulcers treated with Heberprot-P®

Variables	Yes		No	
	No	%	No	%
High blood pressure	15	53,6	13	46,4
Obesity	8	28,6	20	71,4
Ischemic heart disease	5	17,9	23	82,1
COPD	3	10,7	25	89,

Table 2 shows that among the personal medical history of the group of diabetic patients studied, high blood pressure is present in 56,3 % of the sample, followed by obesity in 28,6 % of the patients investigated.

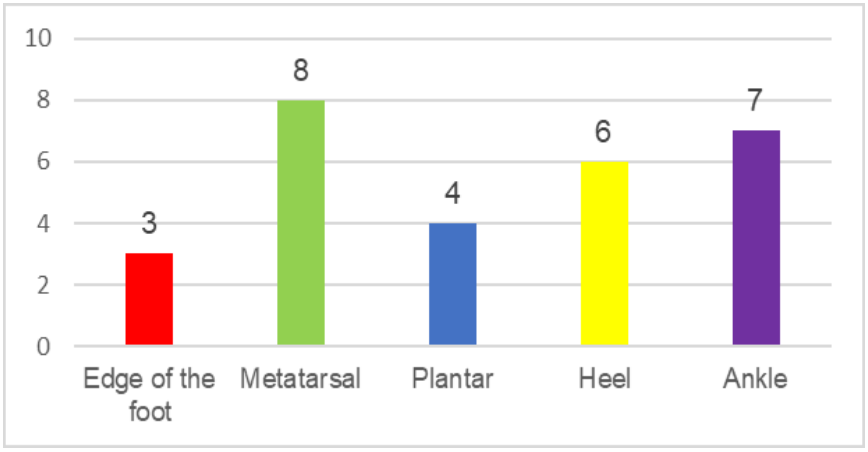


Figure 2. Anatomical location of diabetic foot ulcers

Figure 2 shows that the most common location of ulcers in the study group is the metatarsal region, with eight patients.

Table 3. Sample Distribution according to wound healing time

Healing time (months)	No	%	Mean	Minimum	Max
From 1 to 2 months and 30 days	17	60,7			
3 to 4 months and 30 days	7	25	2,64	1,0	6
From 5 to 6 months and 30 days	4	14			

Table 3 shows that 100 % of the patients studied had diabetic foot healing, the majority of them (60,7 %) within 3 months, with a minimum of one month and a maximum of 6 months.

Table 4. Comparison of healing time taking into account pathological history and toxic and dietary habits

Variables	Healing time (months)		Mann Whitney U test (p)
	Yes	No	
	Mean	Mean	
High blood pressure	2,5	2,8	0,7
Obesity	2,8	1,5	0,01
Smoking	3,2	1,	0,04
Ischemic heart disease	2,9	2,6	0,98
COPD	1,7	2,8	0,64
Nutrition	Inadequate	Adequate	0,04
	3,1	1,0	

Table 4 shows that when applying the Mann Whitney U test, it was observed that in patients with obesity, smoking, and an inadequate diet, the healing time of the lesion was significantly longer than in those without such a history, with 95 % certainty.

Table 5. Association between age and healing time

Variables	Pearson correlation	
	Correlation coefficient	p
Age (years) Curing time (months)	0,52	0,00

Table 5 shows that there is a statistically significant association between patient age and healing time with a p<0,05. This relationship is direct, as healing time increases with patient age.

DISCUSSION

Diabetes mellitus is one of the greatest challenges in the field of chronic diseases, with an explosive increase in type 2 diabetes due to population growth and aging, increased obesity, poor eating habits, and a sedentary lifestyle.[17],

The predominance of patients over 70 years of age and females can be attributed to the higher frequency of diabetes mellitus after the sixth decade of life and in females, according to Cuban statistics.[19] In addition, this complication of diabetes tends to appear in patients with a long history of the disease and even more so with previous vascular disorders.

Age is recognized in various literature as an important risk factor for chronic non-communicable diseases such as HTN and DM.[18]

Other authors, such as Medina and Carbajales[19] agreed with the predominance of patients in the 65-74 age group and females. Similarly, Camaño et al.[15] found a higher number of females and patients in the 60-69 age group. Other studies published similar results.[17,20,21]

The higher number of patients with white skin color corresponds to the characteristics of the Cuban population, where this skin color predominates.

Camacho et al. also found a predominance of patients with white skin color.[22]

The predominance of hypertension and obesity corresponds to the incidence of these diseases worldwide and in Cuba. Globally, more than one in five adults has high blood pressure. The prevalence of hypertension worldwide in 2019 was highest in Central and Eastern Europe, Central Asia, Oceania, Southern Africa, and some countries in Latin America and the Caribbean.[23]

Research addresses the high frequency of diabetic patients with hypertension and/or obesity.[24] Seguí and colleagues point out that there is a significant association between obesity, sedentary lifestyles, and dietary transgressions as risk factors for diabetes mellitus.[25] Mata also points to these risk factors as important predisposing factors for developing the disease, especially after the age of 50.[26]

The presence of lesions predominantly in the areas indicated could be due to the use of inappropriate footwear for these patients, as these are areas exposed to friction with footwear. Scholars on the subject report that the constant use of footwear with proven plantar pressure relief prevents the appearance and/or recurrence of plantar ulcers, specifically recurrent ulcers on the plantar surface of the metatarsal heads.[27]

Different studies have reported favorable outcomes with up to 100 % healing of the lesion with the use of Heberprot-P®.[16,28] López et al.,[20] also highlight the effectiveness of Heberprot-P® in achieving high healing rates and preventing amputations.

The results presented in relation to healing time, taking into account pathological history, toxic habits, and diet, can be related to the effects of obesity, smoking, and poor nutrition, the latter being closely related to metabolic control, on blood vessels and the immune system, which hinder adequate tissue irrigation and healing.

Martínez[29] also reports an association between overweight or obesity and diabetic foot. González Lozada published similar results.[30] Agurto Cruz,[31] concluded that overweight or obesity increases the risk of complications in patients with neuropathy and diabetic foot by 52 %, these being the most complex, demonstrating the ineffectiveness of pharmacological treatments. As evidenced in the study.

CONCLUSIONS

The study sample was predominantly made up of patients over 70 years of age, female, and white. High blood pressure and obesity were the most common medical conditions. The most frequent location of ulcers is the metatarsal region, followed by the ankle region, with most of these lesions healing within 3 months. The healing time of the lesion shows a statistical relationship with the presence of obesity, smoking, and an inadequate diet. It is also observed that as the patient's age increases, the healing time of the lesion also increases.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHOR CONTRIBUTION

Conceptualization: Sergio Alberto Díaz Cruz, Talia Batista Villar, Doraimys Valido-Valdes, Ymirsys Núñez Núñez, José Luis

Fernández González.

Data curation: Sergio Alberto Díaz Cruz, Talia Batista Villar.

Formal analysis: Sergio Alberto Díaz Cruz, Talia Batista Villar, Doraimys Valido-Valdes, Ymirsys Núñez Núñez, José Luis Fernández González.

Research: Sergio Alberto Díaz Cruz, Talia Batista Villar, Talia Batista Villar, Doraimys Valido-Valdes, Ymirsys Núñez Núñez, José Luis Fernández González.

Methodology: Sergio Alberto Díaz Cruz, Talia Batista Villar, Doraimys Valido-Valdes.

Project management: Sergio Alberto Díaz Cruz.

Resources: Ymirsys Núñez Núñez, José Luis Fernández González.

Supervision: Sergio Alberto Díaz Cruz.

Validation: Sergio Alberto Díaz Cruz, Doraimys Valido-Valdes.

Visualization: Sergio Alberto Díaz Cruz.

Writing – original draft: Sergio Alberto Díaz Cruz, Talia Batista Villar, Doraimys Valido-Valdes, Ymirsys Núñez Núñez, José Luis Fernández González.

Writing – review and editing: Sergio Alberto Díaz Cruz, Talia Batista Villar, Doraimys Valido-Valdes, Ymirsys Núñez Núñez, José Luis Fernández González.

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