

ORIGINAL ARTICLE

Health-related quality of life in patients with diabetic foot with heberprot-P therapy

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ABSTRACT

Introduction: little research has addressed the relationship between the impact of the drug heberprot-P in medical treatment and the quality of life of patients with diabetic foot ulcers.

Objective: to determine the health-related quality of life of patients with diabetic foot ulcers treated with heberprot-P at the Policlínico “Capitán Roberto Fleites” according to the SF-36 questionnaire.

Methods: an observational, descriptive, longitudinal, descriptive study was conducted in patients attended at the “Capitán Roberto Fleites” Polyclinic from January to December 2018. Seventy-seven patients with heberprot-P treatment were studied to learn about both positive and negative states of physical health and emotional well-being covering the scales: physical function, physical role, bodily pain, general health, vitality, social function, emotional role and mental health at three points in time.

Results: patients older than 70 years, female sex, type 2 diabetes and superficial ulcer (Wagner I) predominated. Heberprot-P was effective in achieving high healing and avoiding amputations. The dimensions social function, vitality and mental health obtained the lowest scores since the beginning of the investigation. The other dimensions improved as the treatment was carried out.

Conclusions: the results allow affirming that the social function, vitality and mental health dimensions compromised the health-related quality of life. It was evidenced that the components of mental health and physical health, as well as health-related quality of life, obtained good scores at the end of the evaluation.

Key words: diabetic foot; Heberprot P; quality of life

RESUMEN

Introducción: son escasas las investigaciones que han abordado la relación entre el impacto del medicamento heberprot-P en el tratamiento médico y la calidad de vida de los pacientes con úlceras del pie diabético.

Objetivo: determinar la calidad de vida relacionada con salud de pacientes con úlcera del pie diabético tratados con heberprot-P en el Policlínico “Capitán Roberto Fleites” según el cuestionario SF-36.

Métodos: se realizó un estudio observacional, descriptivo, longitudinal en pacientes atendidos en el Policlínico “Capitán Roberto Fleites” desde enero a diciembre de 2018.

Se estudiaron 77 pacientes con tratamiento con heberprot-P para conocer de estados tanto positivos como negativos de la salud física y del bienestar emocional que cubren las escalas: función física, rol físico, dolor corporal, salud general, vitalidad, función social, rol emocional y salud mental en tres momentos.

Resultados: predominaron los pacientes mayores de 70 años, el sexo femenino, la diabetes tipo 2 y la úlcera superficial (Wagner I). El heberprot-P resultó efectivo al lograr una alta cicatrización y evitar las amputaciones. Las dimensiones función social, vitalidad y salud mental obtuvieron las más bajas puntuaciones desde el inicio de la investigación. Las demás dimensiones mejoraron en la medida en que se realizó el tratamiento.

Conclusiones: los resultados permiten afirmar que las dimensiones función social, vitalidad y salud mental comprometieron la calidad de vida relacionada con la salud. Se evidenció que los componentes de salud mental y salud física, así como la calidad de vida relacionada con salud, obtuvieron buena calificación al final de la evaluación.

Palabras clave: pie diabético; Heberprot P; calidad de vida

INTRODUCTION

Foot disorders are the most common cause of hospital admission in people with diabetes mellitus (DM) and one of the main causes of morbidity and disability, with important biological, psychological and social repercussions because it reduces the quality of life of those affected.⁽¹⁾ Of these disorders, the diabetic foot (first reported in 1887 by the surgeon Pryce) is one of the chronic complications of DM that can lead patients to suffer amputations of their lower limbs, with the psycho-social damage that this entails.⁽²⁾

In the health institutions of Villa Clara Province, in the period between the years 2017 and 2021,⁽³⁾ more than 4 206 patients with diabetic foot ulcer (DFU) have been attended - a figure that tends to increase over the years -, who have been given heberprot-P with good results. Specifically, 197 patients have been treated at the "Capitán Roberto Fleites" Polyclinic during this period. The review of the scientific literature recognizes that the importance of heberprot-P is justified because with the injection in the wounds the patients have a quicker recovery, the days of admission decrease and there is no hospital stay, the Public Health obtains savings and the patient and the family benefits and improves the quality of life of the patients;^(4,5,6,7) for these same reasons the investigations related to this drug register positive results.

There are few investigations that have addressed the relationship between the impact of the drug on medical treatment and the quality of life of patients. In 2017, a study was initiated with diabetic patients treated with heberprot-P in the country with the aim of assessing social integration with minimal disability, health-related quality of life (HRQoL) and the efficacy of the product in primary health care; this work is part of that research.

Among the multiple meanings of quality of life (QoL), the one of the World Health Organization stands out, which refers to QoL as a state of general well-being comprising objective dimensions and subjective assessments of economic conditions, physical health, emotional state and social relationships; all permeated by the culture and value system in which one lives.⁽⁸⁾

Health-related quality of life (HRQoL) is that which, when related to health from a subjective perspective, can be understood as the level of well-being perceived by people in relation to their development in their environment,

emphasis should be placed on the impact this has on their health and the measurements that are made based on the individual's own subjective perceptions, such as the SF-36 health questionnaire, which evaluates the quality of life in health.⁽⁹⁾

Patients with chronic disease experience different associated problems, including those of a physical nature, which are a direct consequence of the disease such as pain, metabolic changes, respiratory difficulties, motor limitations and possible cognitive impairments, in addition to complications arising from medical treatments such as nausea, vomiting and pain, among others, and the presence of negative health states associated with secondary difficulties among which are changes in socioeconomic position, job loss, financial insecurity and dysfunctional relationships.

The need for the study of quality of life by the Public Health System in the country is justified from the results obtained with the drug and with the objective of favoring, improving, structuring and maintaining the quality of life of patients, emphasizing the areas in which it may be affected. Hence the need to approach the patient with this chronic disease from its integrality. The aim of this study is to determine the health-related quality of life of patients with diabetic foot ulcer treated with heberprot-P at the "Capitán Roberto Fleites" Polyclinic according to the SF-36 questionnaire.

METHODS

An observational, descriptive, longitudinal study was carried out. We worked with all the patients (77) treated with heberprot-P at the "Capitán Roberto Fleites" Teaching Polyclinic of Santa Clara City, Villa Clara Province, in the period from January to December 2018.

The design considered the application of the SF-36 questionnaire at three moments, with the aim of evaluating the HRQoL with the application of heberprot-P and the evolution of the injuries. The intervention was performed at three treatment time points: first time point (T0), when the drug was applied; second time point (T1), at lesion closure or eight weeks and third time point (T2), six months after application of the drug. Both positive and negative states of physical health and emotional well-being were determined covering the following scales: physical function, physical role, bodily pain, general health, vitality, social function, emotional role and mental health.

Information gathering

The patient information sheet and the informed consent form were used. Information was collected through the SF-36 questionnaire, Spanish version, to determine the HRQoL in the sample. Observation and the documentary review method were also used for clinical-epidemiological variables. The qualitative variables analyzed were age, gender, type of diabetes, Wagner classification and evolution of the lesion.

The SF-36 questionnaire (Table 1) was used to obtain data to estimate the behavior of health-related quality of life (HRQoL). The questionnaire items report both positive and negative states of physical health and emotional well-being. The 36 items of the instrument cover the following scales: physical function (PF), physical role (PR), bodily pain (P), general health (GH), vitality

(V), social function (SF), emotional role (ER), and mental health (MH), which represent the most frequently employed health concepts when measuring HRQOL. In addition to these eight health scales, an item is included that assesses the general concept of changes in the perception of current health status with respect to how it was one year earlier, which is not used for the calculation of the eight dimensions. By aggregating these dimensions, two components are calculated: the physical health component (PHC) and the mental health component (MHC).

Table 1. Dimensions of the SF-36 questionnaire and their meaning

Dimension	No. of items	Meaning
Physical function	10	Degree in which poor health limits physical activities of daily living such as walking, climbing stairs, picking up or carrying loads, and moderate and strenuous exertion
Physical role	4	Degree in which poor health interferes with work and other daily activities, resulting in lower than desired performance or limited type of activities that can be performed or making it difficult to perform
Body pain	2	Measurement in which pain intensity suffered and its effect on usual work and household activities
General health	5	Personal assessment of health status including current status and future prospects and resistance to illness
Vitality	4	Feeling of energy and vitality versus tiredness and discouragement
Social function	2	Degree to which physical or emotional problems resulting from poor health interfere with normal social life
Emotional role	3	Degree to which emotional problems affect work and other daily activities. Consideration is given to the reduction of time spent, decreased performance and dedication to work
Mental health	5	General health assessment. Depression, anxiety, self-control and general well-being are considered

For each dimension of the SF-36 questionnaire, the items were coded, aggregated and transformed into a scale ranging from 0 (worst state of health) to 100 (best state of health) using the algorithms and indications provided by the scoring and interpretation manual of the questionnaire, validated in Cuba by Trujillo et al.⁽¹⁰⁾ It was considered poor (40% of the total possible score of the dimensions is above the mean), fair (41% to 70% of the total possible score of the dimensions is above the mean) and good (71% to 100% of the total possible score of the dimensions is above the mean).

Statistical analysis

The information obtained was recorded in a data collection spreadsheet in Microsoft Excel and was processed with the help of the statistical package SPSS (Statistical Package for the Social Sciences), version 15.0 for Windows. Contingency tables (frequency and hundreds) were made for qualitative variables.

In the case of quantitative variables, measures of central tendency and dispersion (mean and standard deviation) were used. The mean difference obtained was analyzed using a Student's t-test for one sample. The level of significance was set at $p < 0.01$. The information was presented in tables.

Ethical considerations

The bioethical principles of health research were respected: autonomy, beneficence, nonmaleficence and justice. In this sense, the patients under investigation were able to decide whether or not to participate in the study, as well as to withdraw from it at any stage.

RESULTS

The epidemiological characterization of the sample is shown in Table 2.

Table 2. Gender and age composition

Age range (years)	Sexo				Total	
	Male		Female			
	No.	%	No.	%	No.	%
≤ 30	2	2.6	0	0	2	2.60
31 a 50	4	5.2	5	6.5	9	11.7
51 a 70	20	27.3	21	27.27	41	53.2
71 a 90	10	12.9	13	16.9	23	29.9
> 90	1	1.3	1	1.3	2	2.60
Total	37	48.3	40	51.9	77	100

Source: Patient inclusion registry

Patients with type 2 DM predominated in the study (70, 90.90%). In relation to the distribution of the patients according to the Wagner classification, grade I predominated (44, 57.2%), characterized by a superficial ulcer. The rest of the patients were included 30 (38.9%) in grade II and only 3 (3.9%) were classified as grade III.

The majority of patients (44, 57.2%) required between five and 10 applications of heberprot-P as treatment to achieve healing. 100% of the patients used the 75 µg dose (Table 3).

Table 3. Average number of applications of heberprot-P

No. of applications	No.	%
Less than 5	20	25.9
Between 5 and 10	44	57.2
More than 10	13	16.9
Total	77	100

Source: Patient inclusion registry

In relation to the effectiveness of treatment with heberprot-P in patients with diabetic foot, total healing was recorded in 63 (81.82%), which demonstrates the pharmacological properties of the drug in DFU healing, and partial healing in 14 (18.18%). There were no amputations during the research phase. It is necessary to point out that when performing the evaluations of the percentage of healing, the predominance was total response.

The HRQOL has become a useful indicator of the evolution of health status in patients as an expression of the strategy used by the Cuban Public Health System, not only to prolong life, but also to alleviate symptoms and maintain vital functioning. Based on the previous approach, the behavior of this indicator in patients treated with heberprot-P is analyzed.

The psychometric properties of the eight dimensions of the SF-36 questionnaire and the descriptive values at the time of application of heberprot-P treatment are shown in Table 4. The HRQOL at time zero (T0) was regular, with the lowest value for the social function dimension (47.71%), and the highest score for the physical function dimension (72.61%).

Table 4. Psychometric properties of the SF-36 dimensions and descriptive values

Dimensions	Mean	SD	Median	Range
Physical function	72.61	16.35	73.33	0-100
Vitality	61.69	18.99	60.00	0-100
Pain	69.52	19.74	70.00	0-100
Physical role	71.37	23.51	50.00	0-100
Emotional role	70.85	22.72	50.00	0-100
Social function	47.71	22.87	50.00	0-100
Mental health	61.63	19.60	60.00	0-100
General health	69.09	18.39	75.00	0-100

SD: standard deviation
Source: SF-36 Questionnaire

The SF-36 questionnaire scores obtained by the patients with application of heberprot-P as a function of the time spent in the program are shown in Table 5.

In all dimensions, with the exception of vitality and mental health, highly significant statistical differences are found between the groups ($p < 0.01$) and the result of the Bonferoni tests indicate that the subjects, when they start treatment, show significantly lower scores than at the time of receiving the application of the drug.

The tests show differences between the times in the dimensions of physical function, pain, physical role, emotional role, social function and general health. At the beginning of the treatment, the dimensions of physical role, emotional role and social function showed the lowest values; the first two showed the highest values in the third time, which shows the recovery in these two scales.

Table 5. SF-36 questionnaire scores at the three heberprot-P treatment time points

Dimensions	T0	T1	T2	F	p
	Mean (SD)	Mean (SD)	Mean (SD)		
Physical function	66.0 (13.2)	74.7 (13.3)	77.01 (13.3)	10.62**	0.000
Vitality	64.4 (5.8)	59.8 (27.0)	60.8 (17.8)	1.25	
Pain	88.7 (7.1)	61.8 (17.0)	58.1 (16.5)	105.20**	0.000
Physical role	50.8 (5.9)	70.8 (23.4)	92.5 (14.5)	127.26**	0.000
Emotional role	50.0 (0.0)	69.3 (22.5)	93.3 (10.2)	178.36**	0.000
Social function	20.0 (0.0)	61.0 (18.0)	62.1 (9.6)	320.15**	0.000
Mental health	59.9 (3.2)	59.6 (25.7)	65.4 (21.7)	2.11	
General health	59.2 (25.2)	68.5 (12.9)	79.5 (3.6)	29.38**	0.000

T0: start of treatment; T1: at lesion closure or eight weeks of treatment; T2: six months after drug application

F: prueba F de Bonferoni (análisis de varianza)

**Correlation is significant at the 0.01 level

Source: SF-36 Questionnaire

When analyzing the scores, on average, the population has a self-perception of their HRQOL as the treatment takes effect, from fair to good, rating, of the eight dimensions, four as good for being above 71% and four as fair for being

between scales 41 and 70; the vitality and social function dimensions are the most poorly rated.

Table 6 shows the highly significant correlations between the HRQoL dimensions. In general, correlations resulted between most of the items.

In the case of mental health, it only correlates with general health; however, it is important to note that the items physical role and emotional role have statistically significant correlations with all the remaining items, except with general health. Similarly, it is relevant that pain presents three negative correlations with the remaining items, specifically with physical role, social role and physical function.

Table 6. Spearman's correlation between HRQoL dimensions

	V	D	PR	ER	SF	MH	GH
PF	.349**	-.119	.380**	.336**	.342**	.218**	.020
V		.172**	.315**	.262**	-.011	.373**	.415**
P			-.443**	-.522**	-.326**	-.101	.275**
PR				.802**	.537**	.339**	-.036
ER					.564**	.489**	.091
SF						.044	-.384**
MH							.688**

PF: physical function; PR: physical role; P: bodily pain; V: vitality; SF: social function; ER: emotional role; MH: mental health; GH: general health

**Correlation is significant at the 0.01 level

The HRQOL scores for the physical, mental and total components are shown in Table 7. The HRQOL levels perceived by patients at T2 are higher than at T0, especially in the mental health component (mean T0: 48.6 - mean T2: 70.4); however, the levels shown for MHC are lower than those for PHC ($t=-18.82$; $p<0.000$).

Table 7. Means and standard deviations for physical and mental components and quality of life

	T0		T2		Comparison of samples (Student's t-test)		
	Mean	Standard deviation	Mean	Standard deviation	Difference of Means	T	p
PHC	71.27	4.08	74.05	8.81	-2.78	-3.18	0.002
MHC	48.6	1.489	70.4	10.11	-21.81	-18.82	0.000
HRQOL	59.92	2.20	72.22	8.42	-12.30	-13.91	0.000

PHC: physical health component; MHC: mental health component; HRQOL: health-related quality of life
The correlation is significant at the 0.01 level

When comparing the patients' perception of their HRQOL, it was shown that at T0 it was evaluated as fair and at T2 (six months of treatment) it was evaluated as good.

DISCUSSION

The analysis of the characteristics of the patients included in the study showed a behavior of the disease in terms of age, sex and type of DM similar to that observed in other studies.⁽⁴⁾

According to the sociodemographic characteristics, the average age of the patients with diabetes in the study was 66 years, which coincides with that of other studies that report that type 2 DM has a higher incidence in people aged 40 years or older, something associated with aging processes and inadequate habits throughout life.⁽¹¹⁾

When analyzing health-related quality of life, it is suggested that when a disease is present, the quality of life may be modified by the appearance of symptoms that make it difficult or limit the performance of daily activities, which affects health.⁽¹²⁾

The use of the HRQOL concept as a measure of the patient's perception of his or her level of well-being makes it possible to understand from the perspective of the subjects themselves the evaluation of their own state of health and allows its emerging use and to delve into the vast field of the subjective dimension of human health.

The results are consistent with qualitative studies that have confirmed clinical observations that DFU has an enormous negative psychological and social effect, including reduced social activities, increased family stress for patients and caregivers, limited employment, and financial hardship.⁽¹³⁾

The results reflect that DFU affects more the emotional health component at the beginning of treatment, with higher scores at the end, expressing that the treatment improves their emotional side or at least they do not attribute a deterioration of it to their disease.

Similar results have been obtained in patients with CKD, with an average MHC score significantly lower than the CFM.⁽¹⁴⁾ This indicates that patients with CKD on HD perceive and are aware of the physical limitations derived from the disease.

When evaluating the HRQOL in patients with type 2 DM with the SF-32 questionnaire, the lowest averages were found in the dimensions vitality, general health and bodily pain,⁽¹⁵⁾ which reflects that, in a certain way, the disease makes both groups feel a decrease in their vitality, perception of health worse compared to other people who do not suffer from the disease.

Another study shows that the dimension that presented a greater and significant number of missing values was bodily pain, with a total of 66, as a result of the specification of skipping this item in the case of not having felt pain in the last four weeks.⁽¹⁶⁾

The vitality and social function dimensions obtained the lowest scores. The results do not coincide with those reported in a study in which the dimensions vitality - 66.9 (21.6) -, social function - 76.7 (23.4) - and mental health - 71.1 (20.7) - were higher. (17) They were lower than those obtained in this research in physical function - at 74.6 (23.1) -, role due to physical aspect - at 73 (37.4) -, general health - at 58.6 (20.2) - and role due to emotional aspect - at 68.5 (41.6) - when studying the influence of lifestyle and functionality on health-related quality of life in Mexican population with compromised health.

In a study on health-related quality of life in patients with rheumatoid arthritis⁽¹⁸⁾ they found greater affectation of physical performance, with 35.3 points, and less in social function, with 67.7.

Research carried out in Mexico⁽¹⁹⁾ to assess the quality of life in adults with type 2 DM in health centers showed impairment in HRQOL, especially for anxiety and worry, as well as for social overload.

The results obtained coincide with those of another study⁽²⁰⁾ which, when evaluating the quality of life in patients with type 2 DM with diabetic neuropathy, obtained statistical significance with practically all the dimensions of quality of life with the SF-36 questionnaire and concluded that it is a factor that affects, to a great extent, the HRQOL of the diabetic.

Sepúlveda and collaborators⁽²¹⁾ used the SF-36 questionnaire, as in this study, in patients with diabetic neuropathy, the results showed a relationship with statistical significance in all the dimensions of the questionnaire, with the exception of bodily pain.

When analyzing the HRQOL, the patients with the lowest averages were those who, in addition to having type 2 diabetes mellitus, had associated complications or other diseases. In the case of the sample studied, the effectiveness of continuous intralesional treatment with heberprot-P® is demonstrated because it achieves complete closure of the lesion, is safe and promotes healing of chronic diabetic foot ulcers.

Age-related impairment negatively influences lifestyle and MHC of the HRQOL and significant effects are found on CSF and on lower limb strength functionality and mobility ability.⁽¹⁶⁾ These results indicate that both MHC and lifestyle are not influenced by the age of the subjects, but CSF is. In the study the results were positive, obtaining higher scores six months after treatment in the mental health and physical health components.

The results coincide with those expressed in a study⁽²²⁾ which states that in patients with type 2 DM one of the main changes, and perhaps the one that causes the greatest deterioration, is the emotional aspect because the person is forced to a process of rapid adaptation that goes through different stages that promote different commonly negative emotions such as fear, anger and anxiety and increases stress levels, known as a stage of mourning, which is a response to the loss of health.

Those with chronic and disabling illnesses go through times that may include symptomatic phases and not knowing the reasons for the symptoms. Then comes the diagnosis, which can frustrate them, as they are faced with an incapacitating disease with no cure. With the passage of time, stages of improvement or worsening may appear; each person experiences these phases differently, and each one will affect them in a particular way, according to factors such as the patient's personality, resilience, age, life plans, caregiver network and daily activities, among other issues particular to each case.⁽²³⁾

The results obtained were positive, with higher scores in most of the dimensions six months after treatment. Likewise, they validate the need for studies that, in addition to curing DFU, also provide information to health personnel about how the patient feels when facing a chronic disease and how this affects his or her daily performance in order to have a better quality of life.

CONCLUSIONS

When determining the health-related quality of life of patients with diabetic foot ulcer treated with heberprot-P at the "Capitán Roberto Fleites" Polyclinic, according to the SF-36 questionnaire, it can be affirmed that the dimensions social function, vitality and mental health compromised the health-related quality of life. On the other hand, it was evidenced that the components of

mental health and physical health, as well as health-related quality of life, obtained good scores at the end of the evaluation.

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CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

CONTRIBUTION OF THE AUTHORS

ALP: Conceptualization, formal analysis, methodology, data curation, writing the initial draft and final version of the manuscript.
TÁV, BMR: Formal analysis, research.
AMA: Data curation, methodology.
LPJ, ACHM: Formal analysis, research.