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ORIGINAL

Behavior of the combined use of plasma and Heberprot-P in diabetic ulcers, Guantánamo

Comportamiento del uso combinado del plasma y Heberprot-P en úlceras diabéticas, Guantánamo

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ABSTRACT

Introduction: Diabetes Mellitus is one of the most common diseases. One of its most common complications is diabetic foot; this, in conjunction with other vascular alterations, can lead to amputation. The combined use of Heberprot-P and platelet-rich plasma provides another therapeutic alternative to facilitate healing.
Objective: to determine the behavior of the combined use of platelet-rich plasma and Heberprot-P in diabetic ulcers in the Angiology Department of the "Dr. Agoustinho Neto" General Teaching Hospital, 2025.
Method: a descriptive, retrospective, and longitudinal study was conducted. The sample consisted of (n = 50) patients discharged from the angiology department. Twenty-five patients with neuroinfectious diabetic foot and 25 with ischemic diabetic foot were randomly selected. The variables studied were: healing time, diabetic foot types, healing percentage, and Wagner grade.
Results: 70 % of patients achieved 75 % ulcer healing, of which 42 % were neuroinfectious diabetic foot ulcers. The most common Wagner grade was grade II, at 48 %. Fifty-four percent of patients achieved maximum healing between days 8 and 14. No significant changes occurred during the first week after starting treatment.
Conclusions: neuroinfectious diabetic foot ulcers respond better to treatment with Heberprot P and Plasma. Wagner type II ulcers have a more satisfactory outcome than other ulcers. The use of these treatments reduces healing time by 2 weeks.

Keywords: Heberprot P; Ulcer; Diabetic Foot; Plasma; Healing.

RESUMEN

Introducción: la Diabetes Mellitus es una de las enfermedades más frecuentes. Una de sus complicaciones más comunes es el Pie diabético; esto en conjunto con otras alteraciones vasculares, pueden conllevar a una amputación. El uso combinado del Heberprot p y el plasma rico en plaqueta proporciona otra alternativa terapéutica para facilitar la cicatrización.
Objetivo: determinar el comportamiento del uso combinado del Plasma Rico en Plaquetas y Heberprot-P en úlceras diabéticas en el servicio de Angiología, Hospital General Docente "Dr. Agoustinho Neto" 2025.
Método: se realizó un estudio descriptivo, retrospectivo y longitudinal. El universo se conformó por (n = 50) pacientes egresados del servicio de angiología. Se seleccionaron al azar 25 pacientes con pie diabético Neuroinfeccioso y 25 isquémicos. Se estudiaron las variables: tiempo de cicatrización, tipos de pie diabético, porciento de cicatrización y grado de Wagner.

Resultados: el 70 % de los pacientes lograron obtener un 75 % de cicatrización de la úlcera, de estos el 42 % fueron pie diabéticos Neuroinfeccioso. El Wagner más frecuente fue el grado II con un 48 %. El 54 % de los pacientes obtuvo el máximo de cicatrización entre el 8 y 14 día. Durante la primera semana del inicio del tratamiento no hubo cambios importantes.
Conclusiones: el pie diabético Neuroinfeccioso tiene una mejor respuesta al tratamiento de Heberprot P y Plasma. Las úlceras tipo Wagner II tienen una evolución más satisfactoria que el resto. El uso de estos tratamientos reduce el tiempo de cicatrización en 2 semanas.

Palabras claves: Heberprot P; Úlcera; Pie Diabético; Plasma; Cicatrización.

INTRODUCTION

Diabetes mellitus is considered one of the most prevalent chronic noncommunicable diseases, affecting a high percentage of the population. Within this disease, we find a highly debilitating and dangerous condition: diabetic foot.

A diabetic foot is considered to be any lesion that appears on the foot of a diabetic patient. It is a polymicrobial condition that coexists with other chronic conditions secondary to the underlying disease, which are: neuropathy, macro and micro diabetic angiopathy; these tend to aggravate the patient's condition, leading to amputation, either major or minor.

There are currently many ways to treat diabetic foot, ranging from broad-spectrum antibiotic therapy and debridement of devitalized tissue to the use of new dressings that perform these functions. In Cuba, Heberprot-P is part of the treatment protocol and has proven to be highly effective in preventing major amputations.

Heberprot-P is a medication applied locally directly to the lesion of human epidermal growth factor (FCHrec), improving the formation of useful granulation tissue and healing. One of the first studies was conducted by the National Institute of Angiology and Vascular Surgery with 29 patients with Wagner grade 4 diabetic, ischemic, and neuropathic ulcers, using an intralesional dose of 25 µg. Of these patients, 100 % experienced pain at the application site. This drug is currently registered in 15 countries and has been administered to 100 000 patients.[1]

Given the complexity and prognosis of this condition, innovative therapeutic options have been created to improve healing and prevent major complications in order to provide alternatives for ulcer care. One of these is the use of platelet-rich plasma (PRP), which has been effective in the treatment of multiple conditions. Given its ability to stimulate angiogenesis, cell proliferation, and collagen synthesis, PRP has gained interest as a therapeutic option in wound healing.[2]

There are other ways to treat diabetic foot, although little known, the use of platelet-rich plasma, extracted from the patient themselves, is a novel modality that is rarely used, despite its high rate of rapid healing.

Platelet-rich plasma (PRP) is a blood product with a high platelet content, produced through several successive centrifugations or apheresis.[3] The definition of PRP indicates at least 2,5-1000 x103 platelets/µL suspended in plasma (2 to 7 times the baseline value); lower concentrations will have no effect, and higher concentrations will not increase the biological response or could have inhibitory effects on wound regeneration and decrease angiogenesis.[4,5,6]

To obtain the plasma, approximately 10 ml of blood is first extracted from the patient and placed in a test tube containing approximately 0,5 ml of potassium citrate (anticoagulant); alternatively, sodium heparin can be used. The sample is then left to stand for between 1 hour and 1 hour and a half, during which time the red blood cells can be seen to separate from the plasma, leaving a yellow upper layer (plasma). This layer is extracted and then administered to the patient, either around the healthy skin or intralesionally. The benefits of using platelet-rich plasma locally include: stimulating fibroblast migration, stimulating angiogenesis, and promoting local healing.

PRP has the property of being autologous, as it uses the patient's own blood, which minimizes the risk of rejection or subsequent infections, ensuring patient safety. It is also an easy-to-apply therapy, as it is a relatively simple and quick procedure.[7,8] Some studies have evaluated the antibacterial effects of platelet-rich plasma because it has been shown to contain a variety of antibacterial proteins that enable it to act against germs such as Staphylococcus epidermidis, Escherichia coli, Klebsiella pneumoniae, and methicillin-resistant Staphylococcus aureus, and act synergistically with some antimicrobials.[9,10]

Currently, there are few or no studies on the combined use of Heberprot-P and plasma in the treatment of diabetic foot, this modality being a novel healing method, affordable for the patient, accelerating healing time and reducing hospital stays as well as the risk of major amputation.

The main objective of this article is to determine the behavior of the combined use of Platelet-Rich Plasma

(PRP) and Heberprot-P in diabetic ulcers in the Angiology and Vascular Surgery Service of the "Dr. Agoustinho Neto" General Teaching Hospital during 2025; to provide a theoretical reference that characterizes aspects related to the management and care of diabetic foot ulcers in the province of Guantánamo.

METHOD

A descriptive, retrospective, and longitudinal study was conducted. The universe consisted of (n = 50) patients discharged from the angiology department. Twenty-five patients with neuroinfectious diabetic foot and 25 with ischemic diabetic foot were randomly selected, making up the total population.

The following variables were studied: healing time, types of diabetic foot, healing percentage, and Wagner grade.

To arrive at the results of this research, theoretical, empirical, and statistical methods were applied (frequency analysis for qualitative variables and percentage calculation) based on a dialectical-materialist conception to understand the process under study, its influence on society, and particularly on the patient. Data was also collected through medical records.

To obtain the information, a literature review was conducted on Platelet-Rich Plasma (PRP) and Heberprot-P, through consultation of national (Virtual Library and Health Repositories, Infomed, and Infosol) and international (Lilacs, Pubmed, SCIELO) bibliographic databases. The results of other research on this topic in Cuba, the region, and the rest of the world were also considered. The information collected was processed using the SPSS program. The results were presented in tables. The data were obtained within one month of the first administration of the medication.

The study took into account the principles of the Declaration of Helsinki and the International Committee of Medical Bioethics. Informed consent was not requested from patients because there was no direct interaction with them; the source of information was the medical record.

RESULTS

Table 1. Characterization of the combined use of plasma and Heberprot-P according to the type of diabetic foot and percentage of healing in one month

Type of diabetic foot *	Percentage of healing							
	75 %		50 %		25 %		Total	
	Amount	Percentage	Amount	Percentage	Amount	Percentage	Amount	Percentage
Neuroinfectious	21	42	3	6 %	1	2	25	50
Ischemic	14	28	7	14	4	8 %	25	50
Total	35	70	10	20	5	10	50	100

Note: *Diabetic foot classification according to Mcoock

Table 1 shows that 70 % of patients achieved 75 % ulcer healing, of which 42 % of the total were diabetic foot ulcers Neuroinfectious.

Table 2. Patient behavior according to Wagner grade and percentage of healing

Wagner grades	Percentage of healing							
	75 %		50 %		25 %		Total	
	Amount	Percentage	Amount	Percentage	Amount	Percentage	Amount	Percentage
Grade I	4	8	0	0	0	0	4	8
Grade II	16	32	6	12	2	4 %	24	48
Grade III	7	14	3	6	1	2	11	22
Grade IV	8	16	1	2	2	4 %	11	22
Grade V	0	0	0	0	0	0	0	0
Total	35	70	10	20	5	10	50	100

Table 2 shows that the most frequent Wagner grade was II (deep injury affecting the entire thickness of the skin, including muscle and tendons) with 48 %, and the least frequent was grade V with 0 %. The best healing rate (75 %) was obtained for grade II with 32 %. All grade I ulcers achieved maximum healing.

Table 3. Evaluation of time in relation to the percentage of ulcer healing

Healing time	Percentage of healing							
	75 %		50 %		25 %		Total	
	Amount	Percentage	Amount	Percentage	Amount	Percentage	Amount	Percentage
1 to 7 days	0	0	0	0	1	2	1	2
8 to 14 days	21	42	5	10	1	2	27	54
15 to 21 days	9	18	3	6 %	2	4 %	14	28
22 to 30 days	5	10	2	4 %	1	2	8	16
Total	35	70	10	20	5	10 %	50	100

Table 3 shows that the most common healing time is 8 to 14 days (54 %), with the most common healing percentage being 75 % during this time, representing 42 % of all patients. Only 2 % achieved healing in the first week.

DISCUSSION

The results of the study show that patients with neuroinfectious diabetic foot have a better healing rate than ischemic patients and even a better response to healing when using these medications. It should be noted that this type of diabetic foot (neuroinfectious) has better vascularization than ischemic foot, which allows for a better pharmacological effect. Also, the Wagner classification of diabetic foot that obtained a better response to the combined use of Heberprot P and PRP was grade II, with the majority of this grade achieving 75 % healing in less than a month. It is noteworthy that despite there being few grade I patients, 100 % of them achieved 75 % healing of the ulcer. No healing was achieved in grade V ulcers because these are extensive ischemic lesions with abundant devitalized tissue that generally lead to limb amputation.

During the first week of combined treatment, there were no significant changes in healing; however, starting on the eighth day, improvement in the lesion began to appear. By the second week, more than half of the patients had achieved more than 50 % healing. The satisfactory evolution of the ulcers in a short time is very important, as it reduces hospital stays and minimizes economic losses, both for patients and their families and for the healthcare institution.

There are extensive studies on the use of Heberprot-p and platelet-rich plasma separately, such as Platini et al.[11], who also found similar results, affirm that, compared to conventional treatment, the use of platelet-rich plasma improved wound healing in patients with diabetic ulcers, reduced healing time, length of hospital stay, and amputation rate.[11] These patients progress towards a better quality of life, both physically and mentally.[12] However, no publication has been found on the simultaneous combined use of these two treatments. This study demonstrated the synergy produced by this combination, stimulating angiogenesis and activation of the epidermal growth factor, resulting in rapid healing and a better quality of life for the patient.

CONCLUSIONS

Neuroinfectious diabetic foot responds better to combined treatment with Heberprot-p and PRP. Wagner II ulcers have a more satisfactory outcome than the rest. No improvement was achieved in Wagner V. The use of these treatments reduces ulcer healing time by 2 weeks.

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CONFLICT OF INTEREST

There is no conflict of interest on the part of the authors.

AUTHORS' CONTRIBUTIONS

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