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PLATELET-RICH PLASMA IN VENOUS ULCER HEALING: CASE REPORT

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ABSTRACT

Objective: To evaluate the evolution of tissue repair in venous ulcers treated with platelet-rich plasma. **Methods**: This is a case report with the application of platelet-rich plasma for the treatment of venous ulcers in a specialized clinic in a city in the south of Minas Gerais. At each session, 20 mL of blood was collected and distributed into four tubes with sodium citrate. The blood was centrifuged to extract platelet-rich plasma. Plasma was applied to the wound after cleaning with distilled water and polyhexamethylene biguanide solution. Subsequently, the lesion was covered with gauze impregnated with petrolatum and sterile gauze as a secondary coverage, associated with elastic compression therapy. **Results:** Prior to therapy, the ulcer had an area of 1.18 cm². After five weeks of treatment with platelet-rich plasma, complete healing has occurred. **Conclusion:** Tissue repair occurred after five weeks of treatment without any complications.

DESCRIPTORS: Varicose ulcer. Platelet-rich plasma. Wound healing. Nursing. Enterostomal therapy.

PLASMA RICO EM PLAQUETAS NA CICATRIZAÇÃO DE ÚLCERA VENOSA: RELATO DE CASO

RESUMO

Objetivo: Avaliar a evolução da reparação tecidual de úlcera venosa (UV) tratada com plasma rico em plaquetas (PRP). **Métodos:** Trata-se de relato de caso com aplicação de PRP para tratamento de UV em uma clínica especializada de uma cidade do sul de Minas Gerais. A cada sessão foram coletados 20 mL de sangue distribuídos em quatro tubos com citrato de sódio. O sangue passou por centrifugação para a extração do PRP. O plasma foi aplicado na ferida após a limpeza com água destilada e solução de polihexametileno biguanida. Posteriormente, a lesão foi coberta com gazes impregnada com petrolato e gazes estéreis como cobertura secundária, associado à terapia compressiva elástica. **Resultados:** Anteriormente à terapia, a úlcera apresentava 1,18 cm² de área. Após quatro semanas de tratamento com PRP, ocorreu a completa cicatrização. **Conclusão:** O tratamento mostrou-se eficaz e houve 100% de redução de área.

DESCRITORES: Úlcera varicosa. Plasma rico em plaquetas. Cicatrização. Enfermagem. Estomaterapia.

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PLASMA RICO EN PLAQUETAS EN LA CICATRIZACIÓN DE ÚLCERAS VENOSAS: INFORME DE UN CASO

RESUMEN

Objetivo: Evaluar la evolución de la reparación tisular en úlceras venosas tratadas con plasma rico en plaquetas. **Métodos:** Este es un reporte de caso con la aplicación de plasma rico en plaquetas para el tratamiento de úlceras venosas en una clínica especializada en una ciudad del sur de Minas Gerais. En cada sesión se recogieron 20 ml de sangre y se distribuyeron en cuatro tubos con citrato de sodio. La sangre se centrifugó para extraer plasma rico en plaquetas. Se aplicó plasma a la herida después de limpiarla con agua destilada y solución de polihexametileno biguanida. Posteriormente se cubrió la lesión con gasa impregnada de vaselina y gasa estéril como cobertura secundaria, asociada a terapia compresiva elástica. **Resultados:** Inicialmente la terapia, la úlcera tenía un área de 1,18 cm². Después de cinco semanas de tratamiento con plasma rico en plaquetas, se produjo una curación completa. **Conclusión:** La reparación del tejido ocurrió después de cinco semanas de tratamiento sin ninguna complicación.

DESCRIPTORES: Úlcera varicosa. Plasma rico en plaquetas. Cicatrización de Heridas. Enfermería. Estomaterapia.

INTRODUCTION

Chronic wounds (CWs) are characterized by complex and multifactorial pathophysiology. They present a slowed process of tissue repair and do not progress through the healing phases in an adequate and coordinated way. They repeatedly stagnate in the inflammatory phase[1].

Worldwide, CW is a health problem, since its prevalence represents high rates, with a proportion of 1.15 per thousand inhabitants, generating high costs to the health system, families and patients[2].

Constantly, CWs are associated with distinct morbidities and occur primarily in the lower limbs. They are mainly represented by venous ulcer (VU) (90%), arterial ulcer, pressure ulcer and diabetic ulcer[1–3].

VU affects 1% to 3% of the general population. It is mainly located over the malleoli and is characterized by clinical signs such as varicose veins, hyperpigmentation, edema, telangiectasia, white atrophy, lipodermatosclerosis, superficial wound, irregular edges and large amount of exudate. Complications such as infection and malignancy can occur frequently, which delays healing time and impacts patients' quality of life[2].

In this scenario, nurses are responsible for all stages of care, from welcoming the client, assessing the wound, choosing the treatment and follow-up, to solving the problem[4]. The nursing performance is supported by the Resolution of the Federal Council of Nursing 0567/2018 that regulates the performance of the entire nursing team in the care of patients with wounds[5].

For treating VU, scientific evidence cites the combination of compressive therapy, physical exercise, prescribed medications and dressings according to individual needs[2]. Therefore, the dressing prescription depends on the analysis of the wound characteristics that will guide the professional's action, such as the presence of nonviable tissue, infection or inflammation, exudate and edges[6].

There are different alternatives of advanced therapies on the market, from topical therapy with specific actions to high-tech dressings, such as low-intensity laser, ozone therapy, negative pressure therapy, hyperbaric and autologous therapies such as the use of platelet-rich plasma (PRP)[7,8].

Platelet-rich plasma is a platelet concentrate obtained from autogenous blood. The procedure for its use begins with the application of platelets at the site of the lesion, which form a platelet cap when they adhere to the collagen, activating the growth factors. In this process not only these factors are activated, but also macrophages, osteoblasts, fibroblasts and others, which act together in the physiological process of healing[9].

A systematic review with meta-analysis evaluated the clinical effects of PRP in the treatment of 294 patients with VU. The results ratified that the plasma application accelerated the healing repair period and improved healing rates[10].

A randomized clinical trial looked at the efficacy and safety of the same treatment in VU and corroborated the findings, adding that the procedure is considered safe, effective in healing and pain reduction[11]. Despite the beneficial effects of PRP therapy, both studies report that there are dissimilarities in the protocols for PRP use in wound preparation and use.

Therefore, taking into consideration that it is an innovative, safe, and effective therapy, the objective of this research was to evaluate the evolution of the VU tissue repair with PRP application.

METHODS

This is an exploratory, descriptive case report research conducted from September to October 2021. The research was developed in a clinic specialized in wounds, ostomies and incontinence, located in a city in the south of Minas Gerais.

For patient selection the following inclusion criteria were adopted: age over 18 years, both genders, with venous ulcer (medical and clinical diagnosis), hemogram backdated to three months containing: hematocrit > 45%, hemoglobin > 15 g/dL and platelet count above 150,000/m^3[12]. Only one patient was selected due to the short period of data collection, as this was an undergraduate thesis.

The exclusion criteria were: patients with cases of coagulation disorder, hemophilia, neoplastic lesions, infectious-contagious disease, continuous use of anticoagulant or antiplatelet drugs, and blood transfusion in the last three months.

Two instruments were used for data collection: the first, called Sociodemographic and Clinical Data, was developed in a doctoral thesis on VU[13]. The questionnaire is composed of variables such as gender, age, marital status, level of education, associated diseases, medications in use, wound characteristics, time since onset and wound area; the second, named RESVECH 2.0 (Results Expected from Chronic Wound Healing Assessment), was used to evaluate the evolution of the wound. RESVECH 2.0 is composed of six domains that characterize tissue repair of the wound: size, depth, edges, tissue types, exudate, and infection/inflammation.

There are descriptions about the presentation of the wound at the time of the assessment getting a score for each item. Only the infection/inflammation item has 14 subitems that are individually graded. At the end, to calculate the total value, the points assigned to each domain must be added, thus obtaining the final score of the instrument, which can vary from 0 to 35 points[14].

Outcome variables were obtained before application of the intervention, at the end of the 12-week follow-up, or until VU healing. The primary outcome variable was the regression of the VU area in cm^2 or until complete healing, and was assessed weekly. For this purpose, the wound was photographed with an 8-megapixel digital camera, aperture *f*/2.4, LED flash, backlight sensor, and resolution of 3,264×2,448 pixels, and computerized planimetry (Texas Health Science Center, San Antonio Image Tool, version 3.0, www.ddsdx.uthsca.edu/dig/itdesc.html) was used for calculation. The secondary outcome was the regression of the RESVECH 2.0 instrument score, measured at the beginning and end of treatment.

The selected patient was referred by the surgeon, a partner of the clinic, who was invited to participate and explained the objectives. After his acceptance, he signed the Informed Consent Form.

At the clinic, the patient was referred to the dressing room for the procedure with VU cleaning done by irrigation with sterile water, indicated in research for wound cleansing15,16. Subsequently, a solution of polyhexamethylene biguanide soaked gauze was applied for 15 min to the bed in the wound. After cleaning, the RESVECH 2.0 questionnaire was filled out and the photographic record was taken. This cleaning procedure was performed at each weekly patient return.

For the use of PRP, the manual method was followed, applying it directly to the lesion using a sterile millimeter pipette. After 3 min, the UV was occluded with petrolatum-impregnated gauze, followed by sterile gauze and finished with compression therapy with elastic stockings. The application of PRP was performed weekly by the researchers and at home, when, after training, the patient had two changes of the dressing until the return, in the same way as all the process performed in the clinic, except for the PRP.

For the preparation of the PRP, 20 mL of blood were collected by peripheral venipuncture in the region of the cubital fossa, using a disposable adapter with needle and safety device. The blood was dispensed into vacuum tubes with 3.2% sodium citrate (BD Vacutainer).

The tubes were placed in the CentriBio centrifuge, model SO-2B, for first centrifugation under a force of 2,000 rpm at room temperature at 400 g for 5 min. A sterile millimeter pipette was used to separate the platelets from the plasma contained in the upper part of the tube. This plasma was stored in a container without anticoagulant and again centrifuged at 800 g for 5 min to extract the PRP and platelet-poor plasma. It was automatically observed that the average platelet concentration would be 4 to 5 times higher than the concentration observed in the blood. After the procedure, the PRP was ready for application to the patient, totaling 675,000 μL of platelets.

The survey data was inserted into Microsoft Office Excel 2019 software. Descriptive analysis (measures of position and dispersion) was used for continuous variables and relative and absolute frequency for categorical variables.

The present study respected the precepts established by Resolution 466/12 of December 2012 of the National Health Council. The principles of anonymity, privacy, and professional secrecy were also respected. The research began after approval by the Research Ethics Committee of the Universidade Vale do Rio Verde with consubstantiated opinion No. 4,936,499.

CASE REPORT

Brazilian, male, 57 years old, healthy, mechanic, practicing Catholic, married, father of two children. He reported having a venous ulcer, confirmed by medical report and clinical examination, located on the anterior lower middle third of his right leg for more than two years. Several previous treatments such as ozone therapy, laser therapy, therapies with hydrofibers and foams have been performed without success. No complaints of pain at the moment. He denied smoking, reported being a social drinker on weekends. He did not perform regular physical activity, and ate an average of five times a day, prioritizing fruits, vegetables, eggs, and fish. He took supplements such as magnesium, vitamins D3 and B_{12}, and zinc. Water intake of two liters of water per day and a sleep habit of eight hours per night. He reported present bladder and bowel eliminations with normal aspects. Physical exam: patient lucid, oriented, hydrated, eupneic, acyanotic, height 1.80 m, weight 80 kg, body mass index: 24.7 kg/m^2. He presented a VU in the middle third, anterior face of the right leg with an area of 1.18 cm^2, perilesional with dilated and tortuous superficial veins, hyperpigmentation, dryness, eczema and edema 3+/4+ with characteristics warm, elastic, hard and painless to palpation, capillary filling of 2 seconds, irregular borders and with keratosis, bed with 30% of necrosis and 70% of granulation tissue, serous exudate, yellow, small quantity and odorless.

For the follow-up, planimetry and photographic registration were performed. In the first application, the patient had no episodes of itching, no pain, and no perilesional phlogistic signs. The patient had three VUs, as presented in Fig. 1: the first with an area of 1.18 cm^2, the others were not possible to calculate in planimetry due to the reduced area.

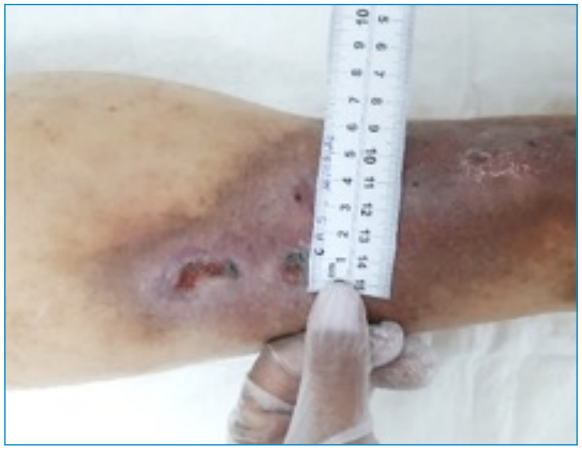

Figure 1. First application of PRP.

Source: Elaborated by the authors.

All applications were photographed and evaluated properly by the researchers. Patient follow-up would be up to 12 weeks or until healing. It occurred that after 29 days of association of PRP, gauze dressings, petrolatum and elastic stockings, the venous ulcers healed, as shown in Figs. 2, 3 and 4.

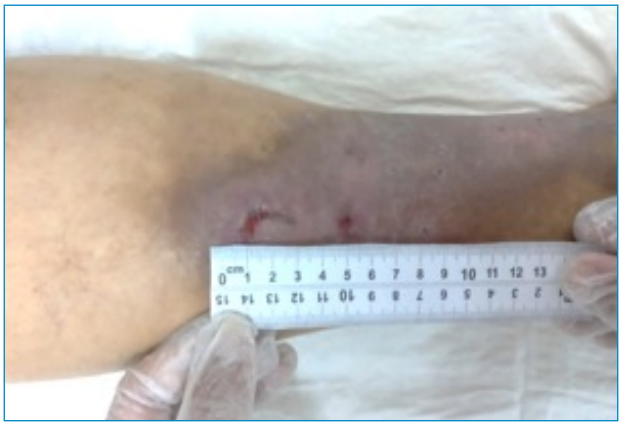

Figure 2. Second week of application.

Source: Elaborated by the authors.

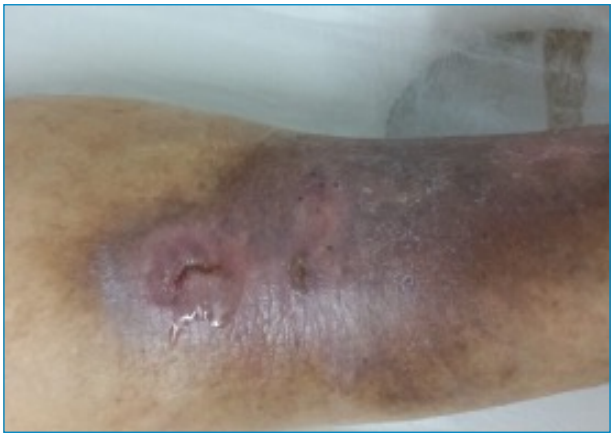

Figure 3. Third week of application.

Source: Elaborated by the authors.

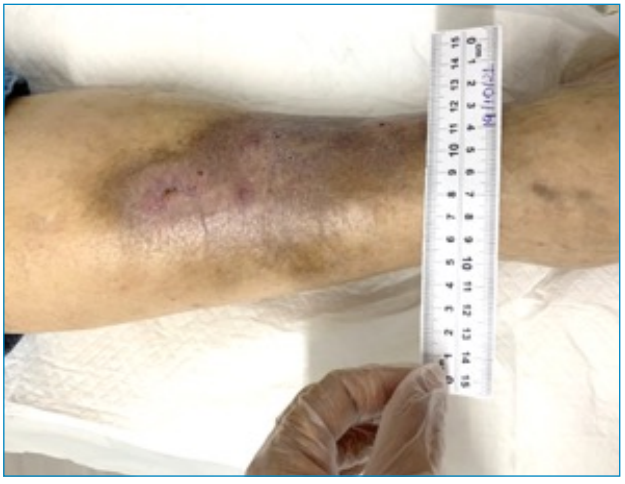

Figure 4. Fourth week of application.

Source: Elaborated by the authors.

As can be seen in Fig. 5, initially the area of the largest VU was 1.18 cm², reducing to 0.07 cm² in the following week. The wound area was calculated using a specific program.

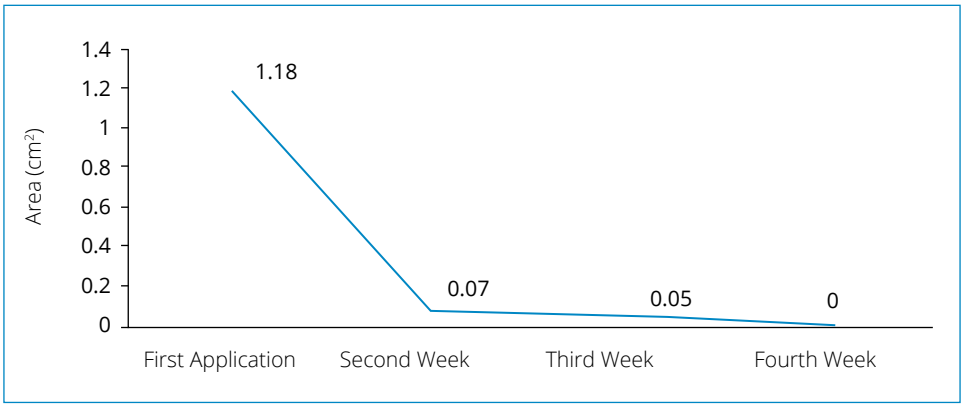

Figure 5. Total VU area in each session.

Source: Elaborated by the authors.

The initial RESVECH assessment indicated an initial score of 18, distributed in the following dimensions: wound area (one point: less than 4 cm²), depth (two points: subcutaneous tissue involvement), margin (three points: damaged), type of tissue in the bed (three points: wet necrosis), exudate (three points: large amount) and inflammation/infection (six points: edema, erythema, friable tissue, stagnant wound, biofilm and satellite lesions). After four weeks of follow-up, the score was zero points, showing complete healing.

DISCUSSION

Regenerative therapies such as the use of PRP have gained prominence in the treatment of wound repair in animals and humans due to the promising results in reducing the healing period. PRP comes from autologous blood, a compound rich in growth factors, cytokines, and cell adhesion molecules[17].

PRP has the purpose of activating several growth factors and more than 30 bioactive structural proteins that act in the healing process, such as: platelet-derived growth factor (PDGF), transforming growth factor beta (TGF-β), vascular endothelial growth factor (VEGF), epidermal growth factor (EGF) and fibroblast growth factor (FGF)[17]. With action in all healing phases, PRP helps inflammation through hemostasis, activating platelet aggregation and the coagulation cascade. Later, in the proliferative phase, it favors granulation tissue formation and angiogenesis, stimulating epithelialization and fibroblast proliferation. Finally, in the remodeling stage, it is involved in wound contraction and collagen deposition[18,19].

In the present study, PRP associated with petrolatum and elastic stocking was promising in VU healing. Although VU presented with a small initial area, a prospective observational study that followed 100 patients with VU, ratified that the action of PRP is independent of size, but had better effect in significantly reducing the area in larger wounds[20].

Such a result corroborates a randomized clinical trial in patients with VU during a four-week follow-up. The group that received PRP showed a reduction of 85.51% of the wound area compared to the control group with a reduction of 42.74%, statistically significant ($p < 0.01$)[21]. Another research compared the use of PRP therapy and conventional treatment (dressing and compressive therapy) in patients with VU for six weeks. The results showed a significant reduction in the area of the intervention group[22].

With regard to the clinical signs of VU measured by RESVECH (size, depth, affected tissues, margins, exudate, and infection/inflammation), PRP therapy showed evolution. A case series study corroborates the results by identifying that there was promotion of the speed of debridement of necrosis and improvement in the appearance of granulation tissue at the 90-day follow-up.

The formation of granulation tissue is a reference in the progression of tissue repair, ordered by collagen and blood vessels, having the function of nourishing the keratinocytes and promoting healing[23].

We emphasize the importance of adequate training and capacity building for the development of the technique and skill in the preparation of PRP for this therapy to be recognized in Brazil, and not only in clinical studies, since the other procedures, such as blood collection and dressings, are routine activities of nurses.

CONCLUSION

The study with PRP associated with gauze, petrolatum, and elastic stockings proved to be effective in treating VU. The wound area reduction at the end was 100%, thus demonstrating significant effectiveness. It is worth noting that controlled research with sufficient sample sizes is needed to prove the effectiveness of PRP in wound treatment.

AUTHORS' CONTRIBUTION

Conceptualization: Moreno DR; Domingues EA; Vallim CA; Silva RS; Fonseca JPS and Noguchi TB; **Methodology:** Moreno DR; Domingues EA and Vallim CA; **Investigation:** Moreno DR and Domingues EA; **Writing - First Draft:** Moreno DR; Domingues EA and Silva RS; **Writing - Review & Editing:** Domingues EA; **Funding Acquisition:** Silva RS; Fonseca JPS and Noguchi TB; **Resources:** Domingues EA; Vallim CA; Silva RS; Fonseca JPS and Noguchi TB; **Supervision:** Domingues EA; Vallim CA; Silva RS; Fonseca JPS and Noguchi TB.

AVAILABILITY OF RESEARCH DATA

All data sets were generated or analyzed in the current study.

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