ARTIGO ORIGINAL

REVISTA ENFERMAGEM ATUAL

Healing Evolution of Chronic Wounds in the Use of Platelet-Rich Plasma: series of cases

Evolução Cicatricial de feridas Crônicas no Uso de Plasma Rico em Plaquetas: série de casos

Natália dos Santos Freitas Maues [1]

Bruna Maiara Ferreira Barreto Pires [2]

Beatriz Guitton Renaud Baptista de Oliveira [3]

Hye Chung Kang [4]

Marilda Andrade [5]

Jane Marcy Neffá Pinto [6]

Pedro Henrique de Carvalho Rodrigues [7]

[1]Nurse. Specialist in Colletive Health. Master student of in Health Care Science in the Aurora Afonso Costa Nursing School (EEAAC), Fluminense Federal University (UFF). RJ, Brazil. E-mail: natifreeitas@gmail.com. Corresponding author.

[2]Nurse. PhD and MSc in Health Care Science in the Aurora Afonso Costa Nursing School (EEAAC), Fluminense Federal University (UFF). RJ, Brazil. E-mail: bruna.barreto@gmail.com.

[3]Nurse. PhD in Nursing. Professor at EEAAC/UFF. RJ, Brazil. E-mail: beatrizguitton@gmail.com.

[4]Pharmaceutical. PhD in Nursing. Professor at EEAAC/UFF. RJ, Brazil. E-mail: hyekang@id.uff.br.

[5]Nurse. PhD in Nursing. Deputy Director and Associate Professor at EEAAC/UFF. RJ, Brazil. E-mail: marildaandrade@uol.com.br.

[6]Physician. PhD in Dermatology. Professor of Dermatology, Department of Clinical Medicine, Faculty of Medicine at UFF. RJ, Brazil. E-mail: janeneffa@gmail.com.

[7]Physician. Specialist in General Surgery and Urology Resident at University Hospital Gafrée Guinle (HUGG/UNIRIO). RJ, Brazil. E-mail: phcr@hotmail.com.

REVISTA ENFERMAGEM ATUAL

Abstract

The aim of this study was to evaluate the effectiveness of Platelet-Rich Plasma (PRP) in the healing process of chronic wounds. This is a cases series study. Primary outcomes: percentage of healed wounds; reduction rate of the wound area. Secondary outcomes: alteration of tissue in the wound bed; amount of exudate from the wound, odor and pain. Data were collected from November 2013 to March 2014, with a follow-up time of 12 weeks. The data collection procedure was performed in three stages: anamnesis, blood collection and treatment and dressing using PRP. The sample consisted of 5 patients with leg ulcers. There was a completely healed wound and the remaining wounds presented an area reduction rate of 34%, 30%, 12% and 11%. It is concluded that PRP favored the tissue repair process.

Keywords: Injury and Wounds; Healing; Growth Factor Derived from Platelets.

Resumo

Objetiva-se avaliar a efetividade do Plasma Rico em Plaquetas (PRP) no processo de cicatrização de feridas crônicas. Trata-se de um estudo de série de casos. Desfechos primários: percentual de feridas cicatrizadas; taxa de redução da área das feridas. Desfechos secundários: alteração do tecido no leito das feridas; quantidade de exsudato da lesão, odor e dor. Os dados foram coletados entre os meses de novembro de 2013 a março de 2014, com tempo de seguimento de 12 semanas. O procedimento de coleta de dados foi realizado em três etapas: anamnese, coleta e tratamento do sangue e a realização do curativo com utilização do PRP. A amostra foi composta por 5 pacientes com úlceras de perna. Houve uma ferida completamente cicatrizada e as demais feridas apresentaram taxa de redução da área de 34%, 30%, 12% e 11%. Conclui-se que o PRP favoreceu o processo de reparo tecidual.

Palavras-chave: Ferimentos e Lesões; Cicatrização; Fator de Crescimento Derivado de Plaquetas.

REVISTA ENFERMAGEM ATUAL

Introduction

Chronic wound is the lesion whose healing process did not occur within 12 weeks[1]. Ulcer is the term used to refer to spontaneous or traumatic wounds, usually in the lower extremities, that do not heal within a reasonable time, with an underlying etiology that may be related to systemic disease or local disorders[2].

Chronic ulcers have a major impact on patients' quality of life and on public health costs in Brazil and in the world. It is considered a serious and worldwide problem. Among lower limbs wounds, vasculogenesis is the most prevalent, characterized by a chronic, painful, recurrent process, with a negative impact on the quality of life, mobility, emotional state and functional capacity of people affected[3].

Furthermore, the concern with the ulcer's treatment cost is global, as it has a great repercussion on the quality of life of the individual and is an additional source of expenses, due to the pharmacological treatment cost and the products for the dressing accomplishment, affecting the family balance, with psychological and social implications for the patient[4].

Therefore, it noted that chronic ulcers cause a great social and economic impact due to its recurrent nature, and the long time elapsed between its opening and healing.

Chronic wounds require a long time to heal and often recur. Even when properly managed the chances of resorting or even not close are large, some patients in our outpatient clinic that have ulcers with the evolution time of up to 42 years stand out. Because of this, the chronic ulcer patient needs more effective and cheaper treatments, such as Platelet-Rich Plasma - PRP[5].

It is known that the skin restoration occurs through a dynamic, continuous, complex and interdependent process, composed of a series of overlapping phases, called healing[6]. The wounds healing process is complex and triggers an organizational and complex cascade of cellular and biochemical events.

For this, it is necessary to favor local conditions through appropriate topical therapy to enable the physiological process of tissue repair. Among the various substances that can be used in the treatment of ulcers is the Platelet-Rich Plasma (PRP), which is a product derived from the whole blood centrifugation, being rich in growth factors and structural proteins[7].

The release of growth factors by the platelets contained in the PRP can favor the repair of the wounds and enable the quicker return to the functionality, possibly by stimulating neovascularization, which improves the blood supply and provides necessary nutrients for tissue regeneration[8-9].

Thus, studies proving its safety, efficacy and effectiveness are necessary since treatment with PRP is inexpensive and develops fewer allergies because it is an autologous process obtained by centrifuging the patient's own blood. Perhaps because it is a low-cost technique of obtaining and preparing, and easy to execute, has not aroused the interest of the pharmaceutical industry. In addition, the autologous PRP use is an important alternative in cases where conventional treatments were not successful[10].

This study is justified by the fact that PRP is a promising technique, presenting few studies and some still very limited in evaluating its efficacy. Since a clearer view of the healing physiology results in a greater understanding of the pathophysiological processes that make healing difficult. This research is part of the project "Preparation of Platelet-Rich Plasma in and its application in the healing process". The issue of research that guided this study was: the PRP is a topical product effective in healing of chronic wounds.

Given the above, it aims to evaluate the effectiveness of PRP in the healing process of chronic wounds.

Method

Cases serie study with therapeutic intervention of PRP in cutaneous ulcers, performed at the Wound Repair Ambulatory, in the University Hospital Antônio Pedro of the Fluminense Federal University (UHAP/FFU), located on the UHAP ground floor.

The dressing accomplishment and the nursing consultation were provided by teaching nurses, residents of Public Health and post-

REVISTA ENFERMAGEM ATUAL

graduate students. The Unit serves the population registered and belonging to the assigned region. Since then, it has been a regional reference center for the treatment of patients with chronic wounds, besides being a field of theoretical and practical teaching in the discipline of Nursing Foundation I.

The primary outcomes that were observed in the study are: healed wounds percentage and wound area reduction rate. Secondary outcomes: tissue alteration in the wound bed, exudate from the wound, odor and pain.

The population of the Wound Repair Ambulatory is predominantly composed of elderly people with chronic noncommunicable diseases, such as: chronic venous insufficiency, arterial hypertension and diabetes.

The study sample was non-probabilistic, due to the convenience of patients with leg ulcers who met the research criteria of inclusion and exclusion, which were not successful with other therapies. Inclusion criteria: be over 18 years of age without distinction of sex; present wounds with a time of evolution greater than 12 weeks; hematocrit> 34%, hemoglobin> 11g/dL, and platelet counts above 150,000/mm³, confirmed with a blood count with retroactive data of up to 3 months. Exclusion criteria: being pregnant or breastfeeding; have coagulation disorders; to present changes in normal values in the TAP and PTT exams; suspected ulcer malignancy; cognitive alterations; and present irregularities in the frequency of attendance at the consultations.

The data collection procedure was performed in three stages: Step 1 of the patient's anamnesis and filling up the protocol I: for data collection, validated instruments were used for outpatient use containing sociodemographic and descriptive data to assess the patient's clinical status and of the wound. In the first service, the participants were screened, the first-time protocol was filed up for the patients' evaluation and the inclusion criteria were applied. Subsequently, for those participants selected, the Free and Informed Consent Form (FICT) was signed and laboratory tests were requested, such as: complete blood count, TAP, PT, creatinine, platelet counts, anti-HIV, anti- HBSAg , anti-HAV, anti-HCV.

In Step 2 of blood collection and manipulation/treatment: Venous puncture was performed with removal of 20 ml of blood from the patient. This blood was collected in 4 tubes with 3.2% sodium citrate and subsequently the samples were centrifuged for 15 minutes under a rotational force of 1500 rpm at 21 ° C. The PRP was removed from the centrifuge, the PRP was aspirated with the 40x1,2 mm needle and the same amount of Calcium Chloride 0.025 mol/Liter was added, transforming the plasma into an aqueous solution.

In Step 3 of dressing and PRP use: during the dressing procedure, the primary dressing was removed, washed with saline solution and debrided with tweezers and scalpel. Afterwards, the PRP was applied to the wound, the IV gauze was covered with a crepe bandage[13]. As for the planimetry and the photographic record, they were carried out every two weeks to follow up the wounds repair process. After 24 hours, the patients were instructed to remove the dressing and perform daily dressing according to the most indicated product, according to the clinical characteristics of the wounds.

The research data were tabulated and analyzed with simple descriptive statistics and later discussed. The absolute frequency and percentage were performed.

The wound analysis was performed using the Mowa® application to evaluate the effectiveness of the treatment used. However, the application has limitation, since it only evaluates the lesions' face, so it was also performed the wound planimetry.

This research was approved by the Research Ethics Committee of the Faculty of Medicine/University Hospital Antônio Pedro, approved through the No. 396/11 CAAE No. 0412.0.258.000-11. Participants signed the Free and Informed Consent Term (FICT), in compliance with Resolution No. 466/12 of the National Health Council (NHC). The information and anonymity of the subjects involved were kept confidential by the researcher, being his sole responsibility, emphasizing that at any time it was the possibility of withdrawing from the study.

Results

REVISTA ENFERMAGEM ATUAL

The sample consisted of five patients, three women and two men. Of these, three had venous ulcers, one had ulcer in one third of the leg referring to Klippel-Trenaunay-Weber Syndrome (KTWS) and one had a chronic heel ulcer after a failed attempt to apply a skin graft. Follow-up time was 90 days, for a total of 30 visits. Patients were attended once a week, with wound measurement and photographic records performed every 15 days.

The results are presented in two categories: Sociodemographic and clinical profile of patients and Evolution of ulcers under treatment with PRP.

Sociodemographic and clinical profile of patients

The sociodemographic characteristics analysis of the research participants allows to describe that the majority (3) is female and has an age range between 60 and 70 years (4). There is predominance of volunteers who have the high level of education (3), followed by elementary school (1) and high school (1). As to marital status, the majority (3) of the participants were married, active and had an employment relationship. Two participants are retired.

It was also observed that two volunteers (40.00%) had Systemic Arterial Hypertension (SAH) and two (40.0%) had Chronic Venous Insufficiency (CVI) and Systolic Arterial Hypertension (SAH) and one (20.00%) has only CVI.

Evolution of ulcers under treatment with PRP

Five wounds were studied, three of them located in the malleolus, one in thirds of the leg with a time of evolution of more than 10 years and the four wounds presented recurrences. Another volunteer presented a wound in the calcaneus of traumatic origin and an evolution time of 5 months.

Table 1. Evolution of leg ulcers over 90 days in treatment with Platelet-Rich Plasma. Niterói, RJ, Brazil, 2014.

Evolution in cm^2 of the wounds						
Wound	D1	D30	D60	D90	Alteration in cm^2	Alteration in %
Wound 1	50,00	49,00	47,00	44,00	-6,00	Reduction of 12
Wound 2	38,00	30,00	28,00	25,00	- 13,00	Reduction of 34
Wound 3	339,00	300,00	250,00	234,00	- 105,00	Reduction of 30
Wound 4	43,00	40,00	38,00	38,00	-5	Reduction of 11
Wound 5	2,00	1,00	0,50	Healed in 90 days	-2	Reduction of 100

Source: survey data.

Table 1 shows that four (80.00%) of the wounds presented reduction of the area, and one wound (20.00%) completely healed.

As for the granulation tissue, favorable to healing process, presented an average increase of 46.80% from the 1st week to the 12nd week, as shown in Table 2.

REVISTA ENFERMAGEM ATUAL

Table 2. Wounds distribution regarding the amount of granulation tissue. Niterói, RJ, Brazil, 2014.

Wounds evolution regarding the amount of granulation tissue				
Wound	**D1**	**D30**	**D60**	**D90**
Wound 1	52,00%	56,00%	65,00%	70,00%
Wound 2	40,00%	42,00%	71,60%	80,00%
Wound 3	15,00%	80,00%	94,00%	96,00%
Wound 4	20,00%	25,00%	75,00%	80,00%
Wound 5	65,00%	70,00%	75,00%	Healed

Source: survey data.

Epithelial tissue, which represents wound closure, presented an average increase of 33.0%. It should be noted that an ulcer completely healed at the end of treatment according to Table 3.

Table 3. Wounds distribution regarding the amount of epithelial tissue. Niterói, RJ, Brazil, 2014.

Wounds evolution regarding the amount of epithelial tissue				
Wound	**D1**	**D30**	**D60**	**D90**
Wound 1	15,00%	30,00%	30,00%	35,00%
Wound 2	20,00%	20,00%	30,00%	40,00%
Wound 3	5,00%	10,00%	20,00%	30,00%
Wound 4	5,00%	5,00%	10,00%	15,00%
Wound 5	10,00%	40,00%	80,00%	Healed

Source: survey data.

Regarding the exudate amount, the majority (three) of the ulcers presented, at the first visit of the study, moderate amount of exudate. At the last visit, two of the wounds were small and one was healed (exudate absent). In addition, at the end of treatment, there were no patients with substantial amounts of exudate as shown in Chart 1.

Chart 1 . Wounds distribution regarding the amount of exudate. Niterói, RJ, Brazil, 2014.

REVISTA ENFERMAGEM ATUAL

Wounds evolution regarding the amount of exudate				
Wound	Beginning	30 days	60 days	90 days
Wound 1	Moderate amount	Moderate amount	Moderate amount	Low amount
Wound 2	Low amount	Low amount	Low amount	Low amount
Wound 3	Moderate amount	Moderate amount	Moderate amount	Moderate amount
Wound 4	Large amount	Moderate amount	Moderate amount	Moderate amount
Wound 5	Moderate amount	Low amount	Low amount	Absent Healed

Source: survey data.

The wound pain complaint of 4 patients was maintained from the beginning to the end of the treatment. None had edema in the perilesional region and three patients complained of pruritus in the wounds (60.0%). There were no adverse reactions to the product during treatment.

Discussion

In the United States, the chronic ulcers prevalence rate is 2% of the general population[10], in Brazil it is estimated 3%[11].

The study results show a predominance of female and elderly patients. Studies[12-13-14] corroborate with these results and mention as predominant comorbidities the SAH and the CVI.

SAH and Diabetes Mellitus (DM) represent two of the main risk factors, contributing decisively to the worsening of this scenario at the national level[13]. Of the patients followed up in the study, 40% had SAH and none had DM.

In view of this scenario, it was identified that chronic wounds are present in a large part in the adult population reaching more frequently the elderly, due to the fact that acute wounds cannot follow the sequential and ordered healing process[6]. Thus, Brazil is rapidly moving towards a more aged demographic profile characterized by an epidemiological transition, in which chronic-degenerative diseases occupy a prominent place.

Regarding education, one participant had completed primary school, one had completed high school and three had completed higher education. This fact is relevant, because for the higher level of education individuals is easier to understand the needs and guidelines for self-care.

In the patient's distribution by occupation, it is observed that all have an income source, being 3 active participants and 2 retired. This data is relevant, since among the patients who work, many report not being able to rest and adequate diet to their treatment and most of them work for a long time standing, which hinders the healing process, since one of the venous ulcer characteristics is stasis and edema, which accumulate throughout the day[15].

REVISTA ENFERMAGEM ATUAL

Clinically, individuals with venous ulcer experience pain and edema in the legs, which worsen at the end of the day and may be alleviated by elevation of the lower limbs. In general, venous ulcer is irregularly shaped, superficial in the beginning, but may become deep, with well-defined borders and commonly with yellowish exudate. The predominant region of this ulcer type is the lower limbs distal portion, but mainly, in the region of the medial malleolus. The skin around the ulcer may be purple and hyperpigmented (ocher dermatitis), extravasation of red blood cells in the dermis and deposition of hemosiderin within the macrophages[13]. The venous wounds presentation etiology is more common in the extremities, around the malleoli, especially the internal, inferior third of the leg[13].

KTWS is a rare condition that is typically manifested by cutaneous capillary malformations, venous and/or lymphatic anomalies, bone and/or soft tissue hypertrophy associated with arteriovenous malformations. Currently, it is considered a congenital pathology[17]. It is estimated that venous/lymphatic changes reach about 70% and limb hypertrophy only 65% of cases. The clinical manifestations of this pathology usually arise at birth or during childhood[15]. One participant in the research had this syndrome.

In the primary outcomes observed, one wound was healed, with an average healing time of 90 days, and the others had a reduction rate of 34.00%, 30.00%, 12.00% and 11.00%.

At the start of treatment, all wounds had some granulation tissue percentage, three wounds had less than 50.00% of granulation tissue. At the end of 90 days, the five wounds had more than 50.00%, and a wound was completely healed. Regarding the presence of epithelial tissue at the beginning of treatment, all wounds had less than 20.00% epithelial tissue in the ulcer bed. At the end of 90 days, 3 wounds had just over 30.00%.

Study[6] shows that the presented tissue characteristic in the wound is an important indicator of the stage of healing achieved or of any complications that may be present. The granulation tissue, fundamental to the physiological tissue repair process, is a bright, red tissue composed basically of blood vessels and collagen, the top of the capillary arches causes the surface to have a granular appearance, from which comes its name.

The epithelial tissue presented at the edges is thin and rosy and its orientation is towards the center of the wound, leading to contraction and consequent wound closure[6]. Wound healing is a complex process intermediated by signals of molecular interaction involving mediators and cellular events, which is followed by recruitment of mesenchymal cells, proliferation and regeneration of the extracellular matrix. The healing process is a response of innate immunity to tissue integrity restoration and is regulated by a pattern of events that include: coagulation, inflammation, formation of granulation tissue, epithelialization, and tissue remodeling. These events are mediated and modulated by cytokines and growth factors that stimulate and modulate such cellular activities[16].

Another important symptom to be evaluated is pain, which in the study, patients was frequent and of varying intensity and not influenced by the ulcer size. Regarding edema, no participant presented, and three patients complained of pruritus in the wounds.

As study contributions are the assistance, teaching and research. It is believed that the understanding of the studied reality is one of the ways to improve the care given in the public health service, contributing to the excellence of care. The main limitation was the patients recruitment and the reduced number of patients, the long time spent in performing the procedure and the impossibility of making solid statistical inferences because it was a serie of cases.

Conclusion

It has been shown that PRP may be successful in healing wounds that do not close by other treatment techniques. The study presented as results: the increase in the velocity of debridement of devitalized tissues; the improvement in the tissue type in the wound bed, because after 90 days a wound healed, and the others presented more than 50% of granulation tissue and epithelization; in addition to decreasing size by 100%, 30%, 34%, 12%, 11%.

The PRP preparation method was performed by trained nurses, and their preparation

REVISTA ENFERMAGEM ATUAL

and dressing took on average 60 minutes after blood collection. The importance of the development of health technologies that bring benefits and safety to the patient with injuries is emphasized, improving their quality of life. Thus, it is expected that the research data will subsidize the accomplishment of new studies with the sample increased.

References

1- Lund H, Curtin J. Management of a non-healing postoperative wound using a bacteria and fungi-binding mesh. Wounds International, 2014;5(4):20-22.

2- Sebastian KMS, Lobato I, Hernández I, Burgos-Alonso N, Gomez-Fernandez MC, López JL, Rodríguez B, et al. Efficacy and safety of autologous platelet rich plasma for the treatment of vascular ulcers in primary care: phase III study. BMC Family Practice. 2014;15:1-8.

3- Malaquias SG, Bachion MM, Sant'Ana SMSC, Dallarmi, CCB, Junior RSL, Ferreira PS. People with vasculogenic ulcers in outpatient nursing care: a study of clinical and sociodemographic variables. Rev Esc Enferm USP. 2012;19(5):535-541.

4- Dias TYAF, Costa IKF, Salvetti MG, Mendes CKTT, Torres GV. Influence of care and clinical characteristics on the quality of life of patients with venous ulcer. Acta Paul Enferm. 2013; 26(6):529-34.

5- Martinez-Zapata MJ, Martí-Carvajal AJ, Solà I, Expósito JA, Bolíbar I, Rodríguez L, Garcia J. Autologous platelet-rich plasma for treating chronic wounds. The Cochrane Library. 2012;17(10).

6- Oliveira BGRB, Nogueira GA, Carvalho MR, Abreu AM. Characterization of patients with venous ulcer accompanied at the Wound Repair Ambulatory. Rev Eletr Enf. 2012; 14(1):156-63.

7- Boswell SG, Cole BJ, Sundman EA, Karas V, Fortier LA. Platelet-rich plasma: a milieu of bioactive factors. Arthroscopy. 2012;28(3):429-439.

8- Souza MV, Pinto JO, Costa MM, Santos EC, Garcia SLR, Oliveira LL. Quantification of growth factors in equine skin treated with platelet-rich plasma. Pesq Vet Bras. 2014; 34(6):599-612.

9- Demidova-Rice TN, Wolf L, Deckenback J, Hamblin, MR, Herman IM. Human platelet-rich plasma and extracellular matrix - derived peptides promote impaired cutaneous wound healing in vivo. PLoS ONE. 2012;7(2):e32146.

10- PINTO JMN, Pizani NS1, Kang HC1, Silva LA1. Application of platelet-rich plasma in the treatment of chronic skin ulcer - case report. An Bras Dermatol. 2014; 89(4):638-40.

11- Fife CE, Carter MJ. Wounds care outcomes and associated cost among patients treated in US outpatient wound centers: data from US wound registry. Wounds. 2012; 24(1):10-17.

12- Reis DB, Perez GA, Zuffi FB, Ferreira LA, Pogetto MTD. Care for people with venous ulcer: nurses' perception of the family health strategy. REME. 2012; 17(1):107-111.

13- Oliveira FP, Chrizóstimo MM, Barreto BMF, Brandão ES, Brum AKR, Oliveira BGRB. Antimicrobial action of epidermal growth factor on wounds: integrative review. Rev Enferm Atual. 2016.

14- Oliveira BGRB, Castro JBA, Granjeiro JM. Epidemiological and clinical overview of patients with chronic wounds treated in an outpatient clinic. Rev Enferm UERJ. 2013; 21(1): 612-7.

15- Dufau JP, Le Tourneau A, Audouin J, Delmer A, Diebold J. Isolated diffuse hemangiomatosis of the spleen with Kasabach-

Merritt-like Syndrome. Histopathology. 1999; 35:337-44.

16- Pinto JMN, Pizani NS, Kang HC, Silva LAK. Application of platelet rich plasma in the treatment of chronic cutaneous ulcer - case report. An Bras Dermatol. 2014; 89(4):638-40.