ROLE OF PLATELET RICH PLASMA IN TREATMENT OF CHRONIC NON-HEALING VENOUS ULCER

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Abstract

Introduction: Venous ulcers are wounds that are thought to occur due to improper functioning of venous valves, usually of the lower limbs. Considering that PRP is a source of growth factors, and consequently has mitogenic, angiogenic, and chemotactic properties, it represents an adjunctive treatment for recalcitrant wounds. Moreover, PRP provides the wound with adhesive proteins, such as fibrinogen, which are important in wound healing. PRP contain more amount of platelets, cytokines and growth factors which are dispersed in a very small amount of plasma which can be prepared from a sample of centrifuged autologous blood. Application of PRP has been reported to be effective in both acute as well as chronic non healing venous ulcers.

Aim and Objective: To evaluate the efficacy of autologous platelet rich plasma in the management of chronic venous ulcer.

Material and Method: A Prospective study conducted on 100 patients of chronic venous ulcers admitted in Sir T. Hospital Bhavnagar from June 2018 to June 2019 after fulfilled our inclusion and exclusion criteria. PRP then injected intalesionally inside and around the periphery of the wound/ulcer. This process was done once/week for 12 weeks. At every week, the area and volume of ulcer was calculated and photographs were taken.

Result: All the patients showed healing of the ulcer with reduction in size of ulcer more than 90% was observed in 72 patients, followed by 80–90% reduction in wound size in 18 patients after the 12 weeks follow-up. Overall, significant reduction in size of ulcer was observed in all the treated patients.

Conclusion: Autologous platelet rich plasma (PRP) as an autologous method, it is biocompatible, simple, safe, affordable and less expensive procedure in the treatment of chronic venous ulcers. PRP is found to be useful in improving and enhancing the healing process in chronic venous leg ulcers without any side effect.

Keywords: Venous ulcer, Platelet rich plasma

Introduction

The ulcer is a break in the continuity of an epithelial surface that can occur in the skin or mucosa of the alimentary or respiratory passages. It may either follow after molecular death of surface epithelium or its traumatic removal. Venous ulcers are wounds that are thought to occur due to improper functioning of venous valves, usually of the lower limbs. Venous ulcers are the most common form of leg ulcers which has a significant impact on quality of life and work productivity. In addition, the costs associated with the long-term care of these chronic wounds are substantial.[1] Conventional therapies such as dressings, surgical debridement, compression bandage and even skin grafting cannot provide satisfactory healing since these treatments are not able to provide necessary growth factors that can modulate healing processes. An effective intervention must thus modify this environment that impedes healing, and is essential to induce the reparative phase of healing and shorten the prior inflammatory phase. In order to succeed, chronic-ulcer management should have a dual

approach, including both underlying disease and local wound treatment. Consensus exists regarding the key points that should include any strategy that is suggested to enhance natural wound healing.[2,3] However, to date, no robust scientific evidence exists to conclude that any dressing is superior to others, and conventional wound care does not supply the growth factors essential to the wound healing process,[4] which have been proven to be present in platelets. Platelets embedded within blood clots have a main role in the physiological process of wound healing, not only as hemostatic agents but also as regulators of inflammation, angiogenesis, cell migration, and proliferation.[5,6] This biological basis supports treatment strategies that include the application of platelet concentrates on the wound, such as PRP. Platelets are anucleate fragments of megakaryocytes that originate in the bone marrow and travel in the bloodstream for 7–10 days. These cellular elements contain a wide protein content in their secretory granules (dense granules, lysosomes, and mainly α -granules). During the physiological process of wound healing, platelets are activated at the site of injury

with release of growth factors and cytokines over time during fibrin retraction. These proteins can bind to the fibrin matrix and to proteoglycans in the extracellular matrix, with the consequent establishment of a storage pool that can be secondarily released by proteinases. Each growth factor activates certain response pathways depending on the cellular environment. PRP is an autologous product derived from whole blood through the process of gradient density centrifugation, there by concentrating a large number of platelets in a small volume of plasma. Platelets play a major role in the process of hemostasis and later wound healing in any wound. During the process of injury platelets gets initially accumulated and form plug producing hemostasis. later by the action of thrombin, platelet membrane gets depolarised and release of platelet granules which are rich in various growth factors like PDGF, PGR, FGF, interleukins.[7,8] These growth factors aid in the process of wound healing by laying collagen matrix, fibroblast proliferation and early maturation of collagen. The most commonly used technique is to obtain a blood sample from the patients themselves (autologous), but homologous techniques are also a valid option. The blood is centrifuged to separate the platelets from red and white blood cells. Depending on the author, single or double centrifugation under different centrifugation times and speed conditions may be used.[9,10] The objective is achieving highly concentrated platelets and suspended in a small volume of plasma, which is consequently rich in growth factors. The mean blood platelet count in normal individuals ranges from 150,000 to 350,000/ μ L. Although a PRP platelet count of 1 million/ μ L (baseline levels $\times 5$) has been postulated as the ideal therapeutic dose of PRP,[11] others propose that platelet integrity is more important than platelet concentration and suggest that PRP should be defined as the volume of plasma that has more platelets than baseline blood.[12] PRP application in ulcer may be intralesional or topical. Intralesional application of PRP will be limited by extent of ulcer and tolerance of patient regarding to pain due to injection. However, PRP can be given topically as well as combined with intralesionally. Before PRP application, the wound should be cleaned with antiseptic solution and adequately debrided to remove excessive slough. PRP not applied in presence of high amount of necrotic or devitalized tissue. Autologous platelet rich plasma (PRP) is a safe, simple, affordable and less expensive procedure in the treatment of chronic ulcers with reportedly good results. Since, it is an autologous method, it is biocompatible and safe.[13] Aim of study is to evaluate the efficacy of autologous platelet rich plasma in the management of chronic venous ulcer.

Material and Methods:

A Prospective study conducted on 100 patients of chronic venous ulcers admitted in Sir T. Hospital Bhavnagar from June 2018 to June 2019 with the following inclusion and exclusion criteria. Informed written consent was taken from all the patients after explaining the treatment protocol and other options available for them.

Inclusion criteria:

- 1- Venous ulcer with ultrasonographic documentation of venous etiology.
- 2-Ulcers more than 6 weeks duration and patients who had received conventional therapies for at least 6 weeks.
- 3-Ulcer without active infection.

Exclusion criteria: Ulcers with active infection.

Procedure: The non-healing venous ulcers were first debrided adequately to remove excessive slough and the wound surface was cleaned thoroughly with betadine solution. PRP then injected intralesionally inside and around the periphery of the wound/ulcer. This process was done once/week for 12 weeks. At every week, the area and volume of ulcer was calculated and photographs were taken. The ulcers were followed up under the following parameters like size of ulcer [with tape], quality of granulation tissue, no of times application, skin grafting, time taken for complete healing.

Results:

Among 100 patients having venous ulcer treated with PRP injections, 63 were males and 37 were females.

Diagram 1: Number of Patients.

Table 1: Percentage reduction in wound size

Reduction in ulcer size at the end of 12 week follow-up	No. of patient with venous ulcer (100)
>90%	72
81-90%	18
71-80%	05
61-70%	03
<60%	02

All the patients showed healing of the ulcer with reduction in size of ulcer more than 90% was observed in 72 patients, followed by 80–90% reduction in wound size in 18 patients after the 12 weeks follow-up. Overall, significant reduction in size of ulcer was observed in all the treated patients.

Discussion:

Venous leg ulcers are responsible for more than half of lower extremity ulcerations, with overall prevalence ranging from 0.06% to 2%. Multiple therapies have been proposed for their treatment. The most popular form of therapy for venous leg ulcers is virtually identical to the compression bandage introduced by Unna in 1885.[14] However, even though limb compression is considered to be standard care for venous leg ulcers, the use of lower-limb compression is not always feasible and successful.[15] The treatment of venous ulcers also entails substantial costs. PRP is a volume of autologous plasma that has a platelet concentration above baseline i.e., five times more than normal platelet counts.[16] PRP enhances wound healing by promoting the healing process by seven growth factors present in it. They are platelet derived growth factor ($\alpha\alpha$, $\alpha\beta$, $\alpha\beta$), fibroblast growth factor, vascular endothelial growth factor, epidermal growth factor, transforming growth factor. These growth factors are important in modulating mesenchymal cell recruitment, proliferation and extracellular matrix synthesis during the healing process.[17] The main goal of any treatment modality is to obtain wound closure expeditiously. The conventional treatment includes adequate debridement of ulcer, control of infection, re-vascularization of ischemic tissue, and avoidance of undue pressure on the wound. Skin grafting has shown some efficacy, however they are not capable of providing the necessary growth factors to modulate the healing process and are expensive. PRP contain more amount of platelets, cytokines and growth factors which are dispersed in a very small amount of plasma which can be prepared from a sample of centrifuged autologous blood. The α -granules of platelet rich plasma contain various growth factors primarily Platelet Derived Growth Factor (PDGF), Vascular Endothelial Growth Factor (VEGF), Transforming Growth Factor- β (TGF- β), Insulin-like Growth Factor (IGF) and Fibroblast Growth Factor (FGF) to name a few that locally attract progenitor cells to stimulate proliferative and differentiation activities and improve wound healing via autocrine and paracrine mechanisms. Most of venous ulcer heal after definitive therapy like laser, RFA, Foam sclerotherapy but in case of chronic venous ulcer insufficiency, ulcer are to large that persist after definitive therapy. PRP in such ulcer have been found to

be very effective. In our case series, 100 patients with venous ulcer were treated with subcutaneous injections of PRP in and around the wound periphery. All the patients showed healing of the wound with reduction in wound size, and the mean time to healing of the ulcers was 10.5 weeks.

Conclusion:

Autologous platelet rich plasma (PRP) as an autologous method, it is biocompatible, simple, safe, affordable and less expensive procedure in the treatment of chronic venous ulcers. In our study, PRP is found to be useful in improving and enhancing the healing process in chronic venous leg ulcers without any side effect. Thereby using PRP to treat chronic venous ulcers may not only enhance healing process, but also prevent lower extremity amputations thereby reduce the morbidity rate that is caused by large non-healing wounds.

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