REVIEW

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Platelet-rich plasma for chronic ulcers

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ABSTRACT

Ulcers that do not heal for more than 3 months are defined as chronic ulcers. Due to their increasing morbidity and mortality rates, difficulty of treatment, psychological and financial burdens, chronic ulcers are considered as a significant health problem encountered worldwide. Dressings, compression bandages, debridement, skin grafts, and other conventional treatment modalities lack growth factors needed to modulate healing process, thus less healing along with constantly repeated treatments make the whole healing process expensive. Platelet-rich plasma (PRP) is an easy, reasonably-priced modality containing growth factors needed to increase the speed of tissue healing.

Keywords: chronic ulcers, platelet-rich plasma, wound healing.
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INTRODUCTION

A wound that takes over 3 months to heal is defined as a chronic ulcer. These ulcers increase morbidity and mortality rates and become a major health problem worldwide. Local or systemic factors can cause chronic ulcers. There may be as many as 6 million Americans who have chronic ulcers, according to estimates. Meanwhile, the global prevalence ranges from 1.9-13.1%.[1] It is estimated that nearly 10% of the world population will experience chronic ulcers throughout their life, with a mortality rate of 2.5%.[2] Treatment for chronic ulcers aims to heal the wound as soon as reasonably possible. The key to healing chronic ulcers is to determine the underlying etiology, the factors that influence the healing process, and create a suitable environment for healing to treat the wound effectively. Conventional methods for treating chronic wounds are often less effective. Dressings, compression bandages, debridement, skin grafting, and other conventional therapy modalities cannot provide satisfactory cure because they cannot provide the growth factors needed to help the healing process. According to current estimates, only 50% of chronic wound therapies are successful, necessitating ongoing costly treatment cycles throughout the healing period.[3]

The advent of autologous platelet-rich plasma (PRP) recently became a breakthrough for treating ulcers, especially chronic ulcers. Platelet-rich plasma, a simple and affordable procedure provides the growth factors required to hasten tissue repair.[4] Additionally, the start of tissue regeneration involves the production of clots and platelet degranulation, which releases growth factors (GF) required for wound repair.[5] Thus, PRP can be a promising therapeutic modality and offer opportunities for ulcer treatment in the future.

CHRONIC ULCERS

Definition

A systemic origin, chronic ulcers are characterized as spontaneous or traumatic lesions, often on the lower limbs, that do not respond to early therapy or remain despite proper treatment and do not proceed to long-term healing over time.[4] Up to 6 million people in the United States are estimated have chronic ulcers, which are a serious health issue. The incidence in the world varies between 1.9 and 13.1%.[1] With up to 3% mortality rate, it is predicted that about 10% of people will have chronic ulcers in their lifetime. Family history, age, female gender, obesity, pregnancy, long-term standing, and height are risk factors for chronic venous ulcers. The most frequent causes of persistent leg ulcers are venous hypertension and venous insufficiency.[6]

The three primary stages of the natural, dynamic, and intricate wound healing process are inflammation, tissue creation, and tissue remodeling. The absence of growth factors and an increase in the quantity of cytokines that slow the healing process, however, might cause an ulcer to become chronic in nature. The difficulty in healing chronic ulcers lies in the lack of adequate blood supply, long-term repeated stimulation of inflammation in the surrounding tissue, and the presence of dead cavities in the wound.[7]

Oxygen supply and tension around the wound bed area are essential because wound healing needs oxygen to interact with cytokines, which will then supply cells in proliferation. Also, the oxygen also acts as effector for neutrophil respiratory bursts. The course and outcome of wound healing highly depend in the nature of the acute wound, considering its type, size, location, and depth. Chronic wounds may also be worsened by other pathological conditions such as underlying comorbidities. The underlying mechanisms vary widely.

Table 1. Clinical features of common foot ulcers[2]

	Venous	Arterial	Neuropathic
Location	Medial malleolus region	Prominent pressure points, notably around distal foot area	Prominent pressure points
Morphology	Usually shallow, irregular border, yellow in base	Dry and necrotic base, clear demarcation (punched-out lesions)	Punched-out
Surrounding skin	• Brown discoloration due to hemosiderin evaporation • Pinpoint petechiae ("stasis purpura") • Lipodermatosclerosis	Shiny atrophic skin with hair loss	Thick callus
Other findings	• Varices • Extremity/ankle edema • ± Static dermatitis • ± Lymphedema	• Weak/negative peripheral pulse • Prolonged capillary refill time (>3–4 seconds) • Pallor on elevation (45° for 1 minute)	Peripheral neuropathy accompanied by sensational loss ± foot deformity

Table 2. Decubitus ulcer classification based on ICD-10-GM (German modification of ICD-10) 2010[12]

Classification	Description
Grade 1	Reddish pressure zone that doesn't blanch when pressed with fingertips, with skin intact.
Grade 2	Decubitus ulcers (tenderness) with skin erosions, blisters, loss of epidermis and/or dermis (partially) or eventually skin
Grade 3	Decubitus ulcers (tenderness) with loss every layer of skin extending to the subcutaneous tissue damage (necrosis), to the underlying fascia
Grade 4	Decubitus ulcers (tenderness) with necrotic muscle, bone, or other supporting structures like tendons or capsules of the joints

This includes factors that affect the blood supply, immune function, metabolic diseases, medications, or previous local tissue injury. Another essential factors which have important roles in the wound healing process include sustained pressure, temperature, and humidity, all considered external factors.[8]

Types

Venous ulcer, The clinical manifestations of chronic venous illness range widely, from simple varicose veins and telangiectasia to lipo-dermatosclerosis and extensive chronic ulcerations. Patients with venous ulcers often complain of swelling and pain in the legs, usually exacerbated by prolonged standing but improving with leg elevation, use of support stockings or walking, all of which can decrease venous pressure. Venous ulcers are most frequently seen above the medial malleolus. A yellow fibrinous discharge frequently coats the wound bed, and the ulcers are typically shallow with wavy borders. A solid base of non-ischaemic granulation tissue can be visible if the exudate is properly debrided.[9]

Arterial Ulcer, the lack of bleeding is the defining characteristic of arterial ulcers, which are typically rounded in shape with distinct edges. These ulcers frequently develop over bony prominences on the distal lower limb. Significant pain is experienced at the ulcer, and elevating the extremities worsens it. Dorsal pedis artery pulses that are diminished or nonexistent, feet that are chilly and pale when elevated, then turn red when lowered are further symptoms of this decreased arterial perfusion to the legs.[10]

Diabetic/Neuropathic Ulcer, Diabetes ulcers typically develop at bone prominences and high pressure areas, such as the metatarsals, big toes, and heels. The diabetic foot is warm, well-colored, and has a detectable pulse in the absence of peripheral atherosclerotic disease, although it has diminished sensitivity. Charcot feet frequently develop due to foot malformation.[11]

Decubitus Ulcer. The severity of pressure ulcers is classified according to its depth, as can be seen in Table 2. Decubitus ulcers were also assessed based on the location, horizontal length, and condition of the wound. Fistulas, wound pockets, and signs of inflammation should be looked for. Photo documentation and serial measurements are recommended for temporary evaluation of the ulcer course.

Management

The standard treatment modalities currently available for chronic ulcers provide optimum local ulcer wellness. This can be achieved by necrotic tissue debridement, support of a moist wound healing environment, reducing pressure around the wound, antibiotics, antiseptics, or other antibacterial agents for infection control, ischemia management, and other medical comorbidities. A wide range of follow-up care for chronic ulcers includes wound cleansing and treatment with wound dressings, light therapy, skin grafting, vacuum healing therapy, hyperbaric oxygen therapy, platelet-rich fibrin, and surgical therapy including angioplasty and reconstructive surgery.[13-17]

PRP treatment, which is sometimes referred to as an emerging cellular therapy, has drawn interest because of its potential applications in the field of regenerative medicine. PRP functions as a therapeutic agent for many chronic illnesses, which may assist in achieving the highest level of quality care planning. Platelets are suspended in plasma to create autologous PRP, which is made from whole blood. This treatment is well-known for being used to treat persistent ulcers in clinical settings. PRP has 2-6 times more platelet concentrations than the whole blood platelet. Platelets act as physiological reservoirs of various growth factors, with

healing functions, which may help in tissue regeneration.[18]

Platelet-rich plasma for treating chronic ulcers

Definition

PRP refers to blood products obtained after the concentration and separation of whole blood products.[19] Before PRP administration, PRP is usually added with thrombin to activate platelets and produce fibrin gel. Activated platelets can release big amounts of growth factors, which are able to stimulate proliferation and differentiation of cells. These in return may promote reparation of the soft tissue. At the same time, PRP contains a large amount of fibrin. Fibrins are needed for tissue regeneration and contraction, blood clotting, and wound closure.[20]

Mechanism

PRP can induce ulcer healing through hemostasis, inflammation, and angiogenesis regenerative mechanisms. Hemostasis process with autologous fibrinogen/fibrin functioning simultaneously with platelet aggregation and adhesion, platelet-rich plasma emerges as a substitute hemostat. Through its capacity to bind plasma proteins to active platelets, including fibrinogen/fibrin and von Willebrand factor (vWF), GPIIb/IIIa is a key mediator of platelet aggregation. Additionally, it has been demonstrated that a few extracellular matrix substances, including collagen, chondroitin, and hyaluronic acid, interact with or bind to the growing PRP clot (also known as fibrin/platelet gel).[21]

The pro-inflammation process following a tissue damage, apoptosis or necrosis activates tissue repair response pathways, which are then followed by an inflammatory response. By generating chemokines, PRP can influence inflammation and the innate immune system's response. As a chemotactic cytokine that stimulates neutrophils and monocytes, chemokines have the potential to create an inflammatory environment. RANTES (CCL5), PF4 (CXCL4), and CXCL7 (NAP-2) are three major chemokines that are present in platelets and oversee the leukocyte migration program. These chemokines regulate leukocyte behavior and dispersion, especially in relation to damaged tissue.[22]

Neovascularization process through the discovery that platelet activation releases proangiogenic proteins like VEGF, HGF, TGF-1, platelet-derived growth factor (PDGF-A, -B or -C) and other soluble cytokines (such as the chemokines IL-8, angiopoietin, CXCL-12) as well as MMP-1, -2, and -9 supports the theory that PRP regulates angiogenesis. Proangiogenic chemicals affect vascular cell migration, proliferation, and stability overall. Contrarily, PRP offers a number of inhibitors, such as tissue metalloproteinase inhibitors, endostatin, fibronectin, platelet factor 4 (PF4), thrombospondin 1 (TSP-1), macroglobulins, plasminogen activator inhibitor 1 (PAI-1), and angiostatin (TIMP-1–4). A negative feedback mechanism that prevents the angiogenic process from going too far might also activate angiogenesis inhibitors.[18]

Pharmacology

In normal healing of injuries to the musculoskeletal system, the response begins with formation of a blood clot followed by degranulation of platelets. This degranulation then causes the release of growth factors and cytokines that trigger local progenitor cell expansion and chemotaxis of inflammatory cells. Approximately 100% of growth factors are estimated to be released in the first few hours, of which 70% are secreted within the first 10 minutes of PRP activation. Through the administration of PRP, the body's physiological healing process can be enhanced after musculoskeletal injuries. Augmentation of this healing process by PRP has been shown to increase the proliferation of stem cells and fibroblasts. In order for these intact platelets to mediate their effects, they must undergo degranulation. Naturally occurring platelet activation occurs when there is damage to the endothelium. Collagen, thromboxane A2, ADP, and thrombin are all factors that can trigger activation, with thrombin being the most potent activator. Meanwhile, platelet activation in PRP is usually carried out through calcium chloride or thrombin which allows soft adhesion so that it does not have the potential to damage the platelet structure.[23]

PRP has so far been regarded as a secure procedure. Platelet-rich plasma prevents disease transmission and lowers the frequency of immunogenic responses. The technique is therefore quite safe, well tolerated, and has few adverse effects.[23] Clinical trials did not reveal any adverse effects, such as an elevated risk of infection or allergic responses.

Due to its autologous nature, PRP are safe from HIV, hepatitis, and other infectious diseases. However, there have been some recent questions regarding the safety of PRP. Some clinicians state that PRP may increase infection rate due to the use of blood agar, which is mostly used in microbiology for bacterial culture. Even so, PRP are blood clots that form in any wound, so PRP are not able to support bacterial growth. PRP has lower pH of 6.5-6.7 compared to mature blood clots of 7.0-7.2. These findings counter the questions; hence it can be said that PRP inhibits bacterial growth. In addition, calcium chloride and thrombin were used to activate platelets. Some reports of anti-bovine antibody development can cross-react with clotting factors. However, there is little evidence in this cross-reactivity. The lack of usage of bovine thrombin and the removal of bovine factor V contamination from current PRP processing techniques might be the reason of this (200 units). Bovine thrombin is mostly used topically; it does not circulate throughout the body. Sterility may be challenging to maintain during PRP processing, however a number of businesses are already producing clinical autologous platelet concentrate machines, which are small desktop centrifuges utilized at the point of treatment.[24]

In contrary, PRP may have negative effects on cancer patients. PRP may release growth factors in which contribute to tumor development, growth, and metastasis. Because PRP may inhibit and stimulate angiogenesis, further research is needed to help understand the angiogenesis regulation mechanisms triggered by platelets. PRP administration in a pre-existing malignant tumor can trigger neoplastic proliferation of residual cells. This is shown in luminal breast cancer cell proliferation after the platelet-derived growth factor signaling pathway

increases.[25]

PRP therapy should be used with caution since it may have adverse consequences on tumor development and metastasis, even if it is a promising strategy that needs more research. PRP contains a number of angiogenesis stimulators that might aid in the development of tumors. PRP derivatives should be applied cautiously since the release of pro-angiogenic factor-rich platelets can effectively stimulate cancer cell-induced angiogenesis and speed up tumor development in vivo.[25]

Procedure to obtain PRP

The tools and materials needed are blood samples from donors, sterile tubes, syringes, sterile needles, ACD-A anticoagulant, centrifuge, and calcium chloride and thrombin or adenosine diphosphate (ADP) which will produce gel preparations.[23]

The homologous procedure is also a viable alternative to take into consideration. The most typical method to create PRP is to get basic blood from the patient (autologous). Different centrifugation rates are used to separate platelets from erythrocytes and leukocytes; the faster the centrifugation, the more platelets are recovered. Centrifugation is used to produce highly concentrated platelets, suspended in a limited volume of plasma, and rich in growth factors. Key elements influencing the quality and effectiveness of PRP include rotational duration, centrifugation acceleration, and protein separation. A modest rate of centrifugation (almost 100 g, 10 min) in the first round and roughly 400 g in the second cycle to avoid the platelet-activating impact is an effective setting for platelet recovery. Some anesthetics and anticoagulants can change the pH, resulting in a pH that is not ideal for PRP.[23]

Adults typically have blood platelet counts between 150,000 to 350,000/L. Until recently, 1 million platelets per liter of PRP (baseline value multiplied by 5) was thought to be the optimal therapeutic dosage. According to Marx, smaller platelet concentrations couldn't have therapeutic effects. Higher concentrations, however, have not been demonstrated to be advantageous.[26,27] The kind of surgical operation, the level of technical skill

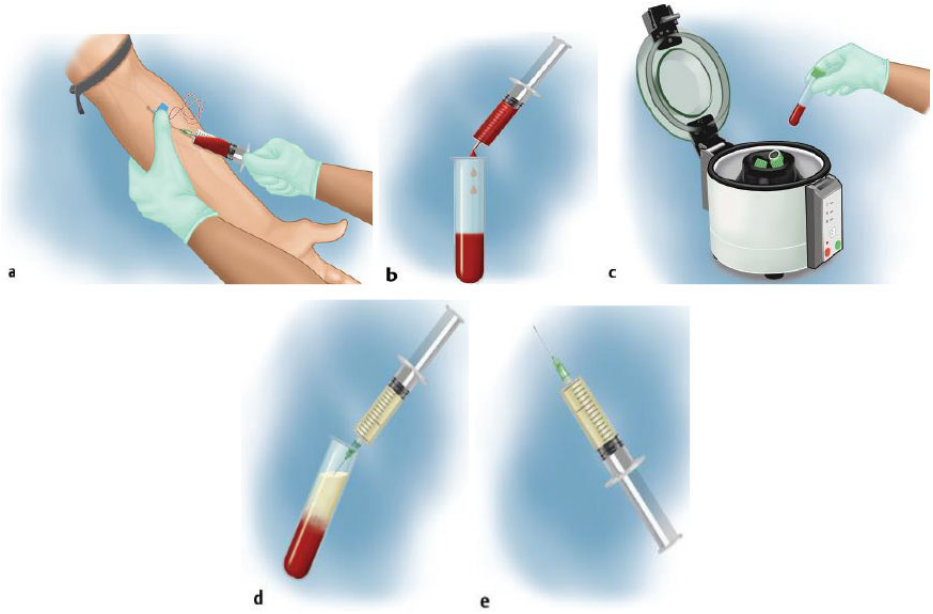

Figure 1. Steps of PRP formation on single spin method. (a) step 1: collection of blood sample from antecubital vein. (b) step 2: transfer of blood to the tube for centrifugation. (c) step 3: specimen is placed on centrifugation device. (d) step 4: PRP extraction to the syringe after centrifugation. (e) step 5: PRP-filled syringe ready to be injected.[18]

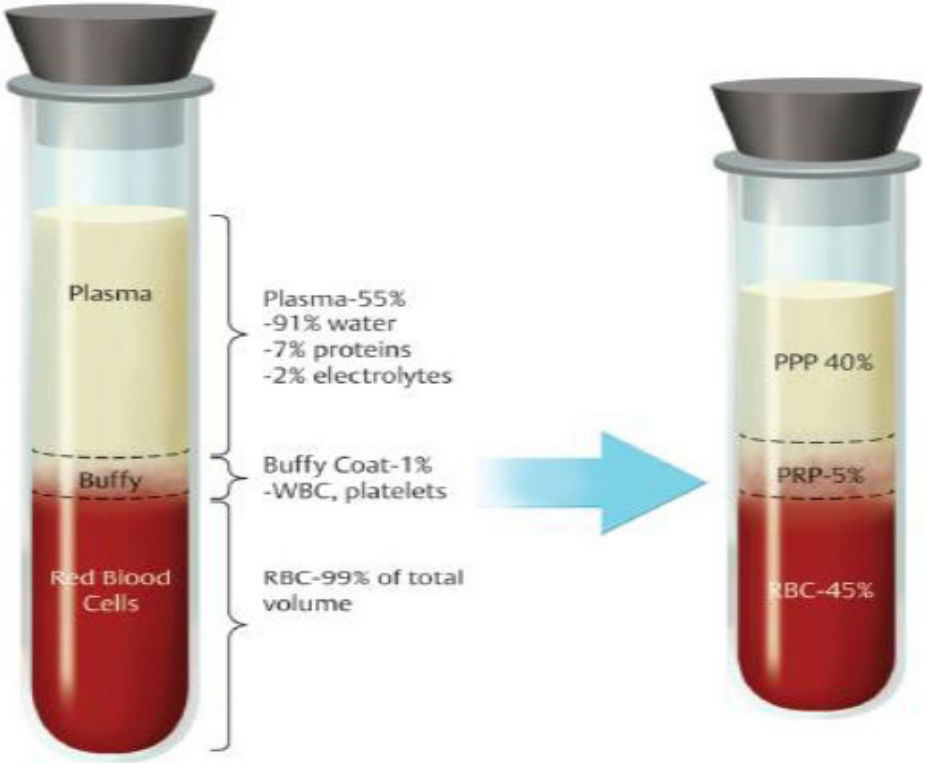

Figure 2. Components of blood and PRP.[23]

available, and the quantity of PRP needed will all influence the sort of device that is used.[28] According to studies, the amount of GF in PRP has dramatically increased. linearly as platelet concentration increases. Giusti et al. reported that a platelet concentration of 1,500,000 platelets/microlitre was necessary for the best stimulation of angiogenesis in endothelial cells. Very high platelet concentrations

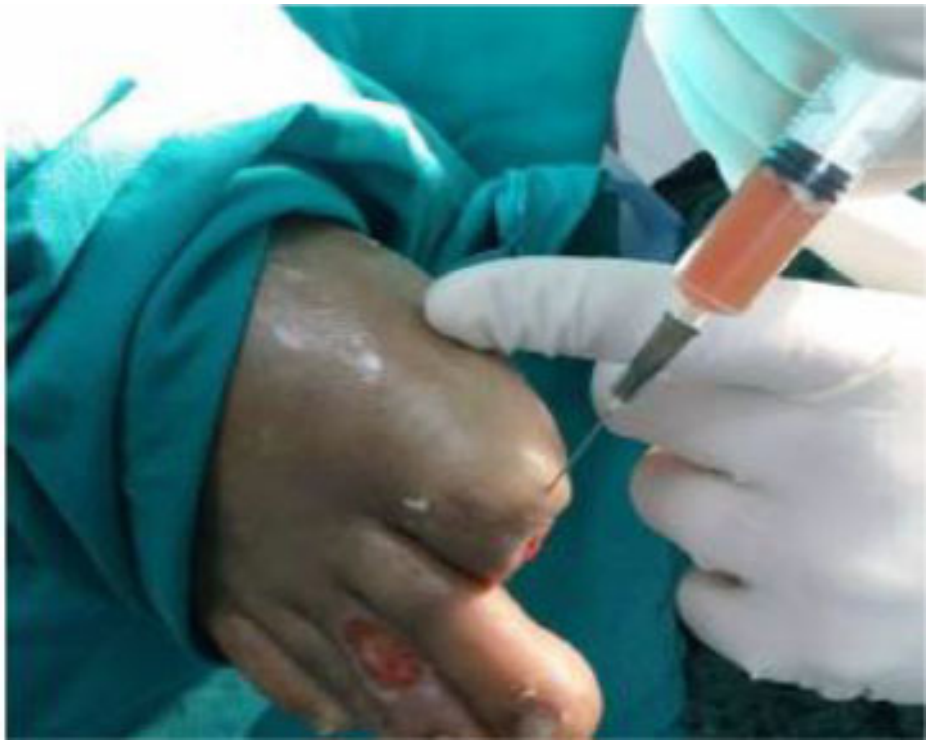

Figure 3. PRP injection to the ulcer.[26]

inhibit angiogenesis.[23,29] Studies that demonstrated the effect of suppressing the process of bone regeneration with extremely high quantities of platelets also found this negative association.[23]

In order to avoid platelet activation and degranulation, venous blood is drawn and combined with anticoagulant citrate dextrose-A (ACD-A). The blood was divided into three layers as a result of the initial centrifugation (slow cycle). Erythrocytes make up 55% of the total volume at the bottom of the tube. Platelet-poor plasma (PPP), which makes about 40% of the total volume at the top of the tube, is a layer of acellular plasma made up mostly of circulating plasmatic molecules and very little platelet content. A layer in between the two has a fast-rising platelet concentration and makes up 5% of the buffy coat's overall volume; this layer will subsequently make up the majority of PRP. A syringe was used to aspirate PPH and PRP, which was subsequently transferred to a tube without anticoagulant. The topcoat and superficial buffy coat were transferred to empty sterile tubes in order to create pure-PRP (P-PRP). The whole buffy coat layer and some red blood cells are removed to create leukocyte-rich PRP (L-PRP). A concentration of platelets results from repeated centrifugation that is longer and quicker (rapid rotation). PRP collection is more straightforward at this point. The majority of the PPH is separated using a syringe, leaving only enough serum for the concentrated suspension of platelets. The device is then given a little shake to make it operational. Then, thrombin or calcium is added to this PRP concentration to activate it, creating a gelatinous platelet gel. Since the system for producing PRP requires only a small amount of blood, no re-infusion is required. Platelet fragmentation during the centrifugation process should be avoided to maintain the integrity of the platelet membrane, ACD-A anticoagulant and low gravity pressure were given during centrifugation. Platelet activation that occurs during this process must be kept to a minimum. Platelet activation may be achieved by adding calcium chloride and thrombin forming a gel preparation, or adenosine diphosphate (ADP). Thrombin activates platelets directly when calcium ions replenish those bound by the anticoagulant ACD-A.[26]

For up to 8 hours, platelet-rich plasma can be kept in a stable anticoagulation condition. Just prior to usage, the calcium chloride solution of thrombin is combined with the platelet content of PRP to trigger the clotting cascade. Within 10 to 15 minutes, the entire process—from activation to factor secretion—is finished. The maximal plasma concentrations of GF are reached during the first 10 minutes. As a result, the process of GF secretion and retention is time-dependent.[26]

Indications

Dermatology, dentistry, plastic and maxillofacial surgery, acute trauma, cosmetic surgery, and veterinary medicine have extensively used PRP treatment. PRP has been used in several trials as a therapy for ligament injuries, tendinopathy, plantar fasciitis, and muscular strains as well as an adjuvant to surgical treatments such rotator cuff repair, restoration of an anterior cruciate ligament rupture, and meniscus repair in knee injury surgery.[20] A study also reports the use of PRP for treating non-healing trophic ulcers in patients with leprosy.[27]

Contraindications

Contraindications to the use of PRP are patients with a history of previous coagulation disorders (such as platelet dysfunction, thrombocytopenia (<100,000), hypofibrinogenemia), patients with hemodynamic instability, septicemia, acute or chronic infections, chronic liver disease, hypersensitivity to bovine thrombin, use of anti-inflammatory drugs. Continuous non-steroidal anticoagulants in the 48 hours before the procedure, injection of corticosteroids into the lesion to be treated or systemic corticosteroids within 2 weeks of the graft procedure, taking anticoagulants or fibrinolytic (warfarin, heparin, and oral anticoagulants such as dabigatran), recently improving fever, cancer especially in the hematopoietic or bone system, anemia with hemoglobin levels <10g/dL, and pregnant women.[28,29]

Side effects

Research by Shahid et al. in 2017 reported several side effects of PRP administration, including dizziness, headache, nausea and vomiting, gastritis, excessive sweating, and tachycardia, which are generally self-limiting. In addition, side effects of PRP administration have been reported such

as post-injection pain, swelling at the injection site, and limitations in activity.[28]

PRP Application

Ehrenfest et al. proposed a classification of PRP preparation, depending on the contents of the cell and its fibrin architecture (Figure 3).

1. Leukocyte-poor PRP products (P-PRP) are preparations that, following PRP activation, have low fibrin network density but lack leukocytes.
2. After PRP activation, leukocyte and PRP products (L-PRP) are preparations with leukocytes but a low density of fibrin network.
3. Products with a high fibrin network density but no leukocytes are known as pure platelet-rich fibrin (P-PRF) or leukocyte-poor platelet-rich fibrin products. P-PRF cannot be injected and is only present in highly active gel.
4. Pure platelet-rich fibrin (P-PRF) preparations or leukocyte-poor platelet-rich fibrin with a high-density fibrin network. These products cannot be injected or applied like conventional fibrin glue; they are only accessible as a highly active gel.
5. Platelet- and leukocyte-rich fibrin (L-PRF). Another name for this product is second-generation PRP. Preparations called L-PRF contain leukocytes and a dense fibrin network.

This classification system is mostly cited, recommended, and validated by a multidisciplinary consensus published in 2012.[30,31,32] In a study conducted by Salem et al. in 2016, PRP and PPP were activated by calcium chloride leading to gel formation for dressings, and PPP was stored for injection. Ulcers were bandaged with fibrin gel on the first day. The procedure can be repeated if no improvements are seen after 2 weeks.[33]

According to one study, PRP was applied following debridement. Initial irrigation of the ulcer site with regular saline solution was followed by sterile gauze wrapping. Basic bandages that were secured using cotton-based tape were then applied to the wound. This procedure was applied three times, separated by five days. Because PRP has a shelf life of up to 7 days, regular saline dressing was utilized instead. There can be a maximum of 10 uses of this technique.[10]

DISCUSSIONS

There is still no standardization of the frequency or duration of PRP therapy. O'Connell's study protocol was that all ulcers were aggressively debrided, then irrigated with sterile 0.9% NaCl, followed by compression dressings 1 week before PRP therapy. PRP application was carried out 1-3 times and observed weekly for 12 weeks.[29] Ficarelli et al. in 2008 applied PRP once a week, and reddish granulation tissue began to be seen after 2 PRP applications. After 20 applications, the ulcer was almost completely healed and complete healing was observed after 1 month of discontinuation of PRP.[34]

Another study demonstrated complete healing in 66.7% of patients with chronic lower leg venous ulcers at 7.1 weeks with a mean of two autologous PRP applications and PRP on a lower leg ulcer that had been present for 3 years in a non-diabetic 65-year-old male patient. After 15 months, the ulcer healed completely, the limbs returned to function and improved the patient's quality of life.[35]

According to a meta-analysis of PRP trials on skin wounds, PRP significantly healed ulcers in tiny, difficult-to-heal acute and chronic wounds compared to wound care as a control. When wounds are treated with PRP, platelets also function as antimicrobials against some skin-surface bacteria, and the likelihood of infection seems to be decreased.[36,37]

One study found that 85 patients (81.7%) showed complete healing with a reduction in wound size of >75% and 13 patients (12.5%) showed a 50-75% reduction in wound size and underwent skin grafting, while six patients (5.7%) showed no healing or reduction in wound size. This rate of ulcer healing treated with PRP was observed at weekly intervals until the fifth week. The mean ulcer area at the most recent visit was 1.69 cm2, which is noteworthy for the research.[10]

Similar research was conducted in 2012 on 20 patients with chronic wounds, of which 10 had profound burns from various sources and 10 had chronic ulcers related to venous, diabetic, and posttraumatic conditions (n = 5, 4 and 1). Ten individuals were split equally between the experimental group, which received PRP therapy three times per week, and the control group, which received standard dressing. On day 28, 2 of the research group's wounds had fully recovered, and 7 wounds had shrunk to an average of 55.5% (range 30.6-85%) of their initial size. All of these wounds had been clinically deemed to have improved. There was still one wound that was infected and was both large and in good condition. In contrast, 3 wounds in the control group were infected, and 6 wounds there had an average size decrease of 21.5% (mean range 7-30%). According to histopathology, the research group's tissue regeneration and epithelialization occurred more quickly than in the control group.[38]

Huber et al. in Brazil performed a different trial on 8 patients with venous ulcers in 2020. These patients received either autologous P-PRP gel or saline solution (control) applied to the lesion on the day of the treatment, weekly, or up to one year following the initial application. All patients received care from a vascular specialist for up to 12 months or until the wounds healed while wearing double compression stockings. A significant reduction in ulcer area showed that pure platelet-rich plasma performed better than saline solution. It is frequently less successful to treat chronic wounds with traditional techniques including mechanical debridement, occlusive dressings, and local medications in the event of infection.[3]

A clinical trial by Helmy et al. in 2021 reported that chronic ulcer treatment with PRP had a faster wound healing ratio (85% within 3 months) compared to conventional dressings (42.5% within 3 months) ($p < 0.01$). In addition, the healing time with PRP was reported to be 2.13 ± 0.48 months, whereas with conventional treatment it was 4.7 ± 4.05 months ($p \leq 0.01$).[39] The trial study also reported similar findings. Clinical Tsai et al. in 2019, who reported that treatment with PRP was able to heal chronic ulcer wounds faster and more effectively.[40]

The effectiveness of PRP is still debatable despite its numerous and extensive applications since there aren't any significant randomized controlled trials and there isn't agreement on how to prepare PRP. Various ulcer etiologies are another factor that needs to be considered in wound healing.[3]

CONCLUSION

Chronic ulcers are spontaneous or traumatic lesions with either a systemic or local underlying cause that do not respond to early therapy and remain after adequate treatment. The traditional approach of treating persistent ulcers has significant drawbacks. As a result, autologous PRP is a significant advancement in the therapy of chronic ulcers since it is a straightforward, affordable, minimally invasive procedure that delivers the essential GF to quicken tissue repair. In the therapeutic dosage range, PRP is safe to use and doesn't have any noticeable adverse effects, according to the available studies. Therefore, PRP has the potential to be a beneficial therapeutic approach, opening up possibilities for the future treatment of soft tissue injuries, ulcers, and several other conditions in regenerative medicine.

CONFLICT OF INTEREST

All author declares that there is no conflict of interest regarding publication of this review.

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AUTHOR CONTRIBUTION

All author had contributed in manuscript writing and agreed for the final version of manuscript for publication.

ETHICAL CONSIDERATION

Not mandatory in review article.

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