

OUR EXPERIENCE WITH THE USE OF PLATELET RICH PLASMA IN NON-HEALING DIABETIC ULCERS

Dr. Sendhil Nathan K^{1*}, Dr. Ashwyn Anand Nelson ² Dr. Vaithiswaran A³ Dr. Prabhu Gunasekaran⁴

1st Author: Faculty, Aarupadai Veedu Medical College, Pondicherry

2nd Author: Faculty, Aarupadai Veedu Medical College, Pondicherry

3rd Author: Assistant Professor, Department of General Surgery, Sri Manakula Vinayagar Medical College, Pondicherry

4th Author: Faculty, Aarupadai Veedu Medical College, Pondicherry

* Corresponding Author : Dr. Sendhil Nathan K^{1*}

Abstract:

In several areas of medicine, including tissue regeneration, platelet-rich plasma (PRP) is frequently employed. Its primary uses in dermatology over the past few years have primarily been in the treatment of wrinkles and wound healing. PRP is a source of growth factors since it has higher concentrations of platelets than whole blood. Chronic wounds are characterised by a protracted inflammatory phase that involves ongoing degradation of growth factors and matrix proteins. The cell migration, proliferation, and differentiation that are necessary for wound healing are facilitated by growth factors. We intend to provide an updated critical assessment of the clinical evidence that supports the utility of PRP for the therapeutic challenge that chronic ulcers represent in this review by outlining the fundamental principles of PRP in wound healing.

Keywords: PRP, chronic nonhealing ulcer, growth, wound healing

Introduction

In healthy persons, wound healing is a very precise and well-orchestrated process, and the ability of damaged tissue to recover is provided by the characteristics of the organisms that support the maintenance of the body's homeostasis. The skin, which accounts for the majority of the body's surface area, is the most vulnerable organ to harm from mechanical trauma, microbial infection, ultraviolet radiation, and extremely high or low temperatures. In order to repair the skin, several cell types and various molecules must be coordinated in four interconnected and overlapping phases: hemostasis, inflammation, proliferation, and remodelling phase.

In healthy persons, wound healing is a very precise and well-orchestrated process, and the ability of the organisms that support the maintenance of the body's homeostasis to repair tissue after harm is what makes it possible.

The skin, which accounts for the majority of the body's surface area, is the most vulnerable organ to harm from mechanical trauma, microbial infection, ultraviolet radiation, and extremely high or low temperatures. In order to repair the skin, several cell types and various molecules must be coordinated in four interconnected and overlapping phases: hemostasis, inflammation, proliferation, and remodelling phase.

Since a prolonged inflammatory phase prohibits the dermal and epidermal cells from responding to chemical agents, wounds that do not heal after an initial insult within a period of six weeks are really classified as chronic wounds. Many systemic and local remedies have been suggested for the treatment of persistent wounds.

Even in high doses, systemic antibiotic therapy is inferior to the antisepsis approach because the medicine do not sufficiently penetrate the wound biofilms. Although the use of antibodies, peptides, hormones, amino

acids, or derivatives has a beneficial effect on chronic wounds, general systemic administration is constrained by challenges in specifically targeting the tissue and the formation of potential side effects.

local treatments, There are also noncellular films and bases (decellularized matrices, porous biopolymer bases, nanofiber meshes, and hydrogels), skin grafts, and dressing therapies available. Despite the large spectrum of potential interventions, many of these therapies are ineffective, expensive, or even experimental, necessitating the development of new and more potent treatments. One of the first methods of regenerative medicine is the use of hemoderivatives, which have been utilised for the past 50 years to treat skin wounds. Many Platelets Rich Plasma (PRP) techniques are still being commercialised today and are used to treat skin wounds. PRP is the first generation of blood concentrates, but the difficulty in getting it and the expense of using it each time a patient receives therapy make

20 patients with chronic or nonhealing ulcers who received autologous PRP therapy from our institution between September 2017 and August 2019 were included in this study after receiving institutional ethical clearance and approval from the head of our hospital to use the records. The patients' ages ranged from 40 to 75.

From prior case files, information on the patient's age, sex, and size of the chronic ulcer that had been present for at least four weeks was gathered.

Patients who were on antiplatelet therapy were instructed to stop taking antiplatelet medication one day before to the procedure. Autologous PRP was made from the patient's blood and centrifuged twice, once for 10 minutes at a speed of 10,000 rpm and once more for 5 minutes at a speed of 5000 rpm.

following centrifugation. After cleaning the wound with normal saline and betadine solution and noting the ulcer's dimensions (length, width, and depth), the chronic ulcer was debrided to remove diseased and dead tissues. Depending on the extent of the incision, autologous PRP was then administered to the chronic ulcer and left alone for 1020 seconds. After that, a sterile, nonabsorbent dressing was applied to the ulcer. Four days following treatment, the dressing was changed, and then once a week after that.

Patients were monitored for 20 weeks, and after the wound was dressed, it was examined for signs of infection and measured to compare to its prior size. The patient was instructed to continue taking drugs for coexisting diseases such as diabetes,

Results

The study included 34 chronic ulcers in 30 patients with 30 different causes who received autologous PRP; the patients' ages ranged from 24 to 65 years, with a mean age of 47.23 years (SD: 13.17). A maximum percentage of cases (33.3%) with a mean age of 47.23 years were in the 51–60 year age range.

There were 30 patients, with a male to female ratio of 2.3:1 and 21 (70%) male patients and 9 (30%) female patients. In the current study, 26 patients (86.7%) had a single ulcer, while 4 (13.3%) had two ulcers. Leprosy-related trophic ulcers (TUs) accounted for 30 (88.23%) of the 34 ulcers, venous ulcers (VUs) for 2 (5.88%), and diabetic ulcers (DUs) for 2 (5.88%).

With a mean of 19 weeks, the ulcer's length ranged from 6 to 48 weeks. For complete healing, 23 instances required 6 PRP sessions, 3 cases required 5 PRP sessions, and the other 4 cases required 4 PRP sessions.

Based on how long they last, ulcers are divided into acute and chronic categories. Patients who have chronic ulcers are at substantial risk of morbidity. In our study population, the lower limbs accounted for the majority of the chronic ulcers, which are linked to underlying diabetes mellitus. Malnutrition, peripheral artery disease, and infection are other factors that increase the chronicity of ulcers.

If there is any obstruction during the aforementioned phases of healing, the wound becomes chronic or nonhealing. The healing of wounds can also be slowed down by conditions like starvation, infection, a systemic disease like diabetes mellitus, and local conditions like arterial disease and venous insufficiency.

PRP is a complex mixture of platelets, cytokines, and various growth factors, such as PDGF (platelet-derived growth factor), which promotes macrophage and fibroblast migration as well as EGF (epithelial growth factor), which promotes fibroblast proliferation and TGF (transforming growth factor), which is mitogenic, chemotactic, and promotes collagen production. In addition, the platelet releases a number of additional substances, including sphingosine

1-phosphate, vitronectin, and fibronectin.

Another benefit of using a single recombinant GF release is the availability of various GF, as was already indicated. The healing of chronic ulcers is aided by these elements. In this setting, autologous PRP therapy offers hope for the treatment of persistent ulcers. Because it requires less advanced techniques and is affordable, PRP therapy can be used successfully in the context of primary care.

In contrast to other techniques like VAC (vacuum-assisted closure), skin grafting, etc., which call for complex techniques, can only be carried out in the context of tertiary or specialty centres, and necessitate hospital hospitalisation. There is no danger of hypersensitivity while using autologous PRP therapy, which can be completed as an outpatient or nursery surgery. And in contrast to other medicines, there is no requirement for frequent follow-up. Additionally, there is decreased risk of infection, negating the need for protracted antibiotic medication. PRP therapy is a promising technique for general practitioners.

A second centrifugation of the patient's blood was necessary to create autologous PRP because RBC interference prevents a single spin from sufficiently concentrating platelets. Autologous PRP therapy is preferable to other methods such as regular wound care and antibiotics, vacuum-assisted closure (VAC), revascularization procedures, skin grafting, etc. because it doesn't cause an allergic reaction or infection. The administration of autologous PRP increased the epithelialization of granulation tissue, which results in the healing of the chronic ulcer, as initially demonstrated by Knighton et al in 1986. This was the first clinical investigation into the potential contribution of local variables on wound healing. In our research, we also demonstrated the healing power of autologous PRP therapy.

Conclusion

Chronic wounds that do not heal with traditional care are common, and treating them presents a significant challenge to the clinician. PRP is an effective alternative therapy for persistent chronic ulcers, and its effectiveness has been proven both in vitro and in vivo. However, more convincing scientific evidence is needed to back up its potential advantages when applied to chronic wounds.

The lack of clinical standards and recommendations is preventing PRP from being used more widely, despite the fact that multiple studies have reported intriguing outcomes with its use to chronic ulcers. Strong clinical trials are necessary to ascertain the most precise indications for usage and the most advised manner of PRP acquisition and application, as several published reviews have previously found. The development of therapeutic protocols and the expansion of PRP use in wound care facilities may have significant socioeconomic effects and enhance the quality of life for patients. The field of regenerative medicine in wound healing is constantly evolving. Its goals are to improve intrinsic regenerative capacity while also supplying necessary components for replacing damaged tissue. Clinical evidence suggests that using a variety of regeneration treatments in combination may improve healing.

References

1. Schreml S, Szeimies RM, Prantl L, Landthaler M, Babilas P. W 2010;63:866–868.
2. Phillips T. Ulceras. In: Bologna JL, Jorizzo JL, Rapini RP, edito 1614.
3. Lazaro JL, Izzo V, Meaume S, Davies AH, Lobmann R, Ucci chronic wound healing: an updated review of clinical evidence.
4. Brölmann FE, Ubbink DT, Nelson EA, Munte AK, van der Hors and systemic wound care. *Br J Surg.* 2012;99:1172–1183.
5. Flanagan M. Principles of wound management. In: Flanagan M, editor. *Wound Healing and Skin Integrity.* Oxford: Wiley-Blackwell; 2013:66–86.
6. Skórkowska-Telichowska K, Czemplik M, Kulma A, Szopa J. The local treatment and available dressings designed for chronic wounds. *J Am Acad Dermatol.* 2013;68:e117–e126.
7. Nurden AT, Nurden P, Sanchez M, Andia I, Anitua E. Platelets and wound healing. *Front Biosci.* 2008;13:3532–3548.
8. Andia I, Abate M. Platelet rich plasma (PRP):underlying biology and clinical correlates. *Regen Med.* 2013;8:645–658.
9. Sánchez M, Andia I, Anitua E, Sánchez P. Platelet rich plasma (PRP) biotechnology: concepts and therapeutic applications in orthopedics and sports medicine. In: Agbo EC, editor. *Innovations in Biotechnology.* Rijeka, Croatia: InTech; 2012:113–138.
10. Kim SA, Ryu HW, Lee KS, Cho JW. Application of platelet-rich plasma accelerates the wound healing process in acute and chronic ulcers through rapid migration and upregulation of cyclin A and CDK4 in HaCaT cells. *Mol Med Rep.* 2013;7:476–480.