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Autologous platelet rich plasma (PRP) for treatment of chronic non healing ulcers of various aetiologies

Dr. Nageswaramma Siddabathuni ; Dr. Silpa Ponnada ; Dr Rakesh Ranen Darla
Guntur Medical College, Guntur, Andhra Pradesh, India
Corresponding Author: Dr. Silpa Ponnada

Introduction: *Chronic non healing ulcers due to diseases like Hansen's, venous insufficiency, diabetes etc. are the major causes for disability. It has been shown that autologous platelet rich plasma (PRP) is effective in healing chronic non healing ulcers.*
Aim*: The objective of this study is to demonstrate the efficacy of autologous platelet rich plasma in patients with chronic non healing ulcers.*
Study design: *Institution based prospective study*
Participants: *Sixteen patients with chronic non healing ulcers of different etiology were taken with a mean age of 48.7years with 24 non healing ulcers of more than 6 weeks.*
Measurements: *photographs were taken before treatment and at every subsequent sitting. Area and volume were calculated at baseline and at every subsequent sitting till the closure was achieved.*
Materials and methods: *Ulcers were treated prior with antibiotics and then those healthy ulcers were treated with PRP injections at weekly intervals, repeated once a week for a minimum of five weeks and extended in case of larger ulcers like those associated with cellulitis as per requirement.*
Results: *The mean percentage of improvement in the area was 65.4 % and volume was 70.2% at the end of second sitting. All ulcers almost closed at the end of five sittings. No adverse events were noted.*
Conclusion: *Autologous PRP for the treatment of chronic non healing ulcers is a feasible, simple, safe and inexpensive method. The growth factors present in autologous PRP helps in a better and faster healing of the ulcers.This method of treatment is a huge step forward in preservation of resources and prevention of morbidity.*

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I. Introduction:

Wounds are at times very complex problem to deal with as it may get associated with chronicity, co-morbidities such as diabetes, non-healing, persistent infections and poor local biology such as loss of sensations. These are very difficult to manage and needs multiple modalities including complex local care such as with negative pressure therapy, antimicrobial dressings; antibiotics and multiple stage surgeries such as debridement, reconstructions with skin gratings, rotational flap or free flaps. [1] Such modalities are associated with further morbidities of the donor site, risks and side effects of pharmacological agents, antibiotic resistance, etc. Ross et al. first described growth factor from platelets. The regenerative medicine as being evolved in this era, offers a strong ray of hope to overcome many diseases. The key regenerative biologic product includes stem cells, mesenchymal cells, and platelets. Platelet as blood products are being used as platelet rich plasma (PRP) and have very promising results for the treatment of various impairments including of tendons and bones. It is also used as local gel application for local care in the treatment of wounds, concurrent (adjunct) to existing wound management practices. The early results, as reported in literature are encouraging

Chronic non-healing leg ulcers are a major health problem. These constitute for 85% causes of leg amputations across the world. needs multiple modalities including complex local care such as with negative pressure therapy, antimicrobial dressings; antibiotics and multiple stage surgeries such as debridement, reconstructions with skin gratings, rotational flap or free flaps. . These are very difficult to manage and Such modalities are associated with further morbidities of the donor site, risks and side effects of pharmacological agents, antibiotic resistance, etc.

These conventional treatments have not shown satisfactory results as these procedures do not provide necessary growth factors required for ulcer healing. Autologous platelet rich plasma (PRP) is an inexpensive method used in treating non healing ulcers as it provides growth factors which enhance healing.

II. Materials and methods:

In this study, 16 patients with 24 ulcers were included with the following inclusion and exclusion from January 2016 to April 2016. Ethical clearance was taken from the institutional ethical committee.

Inclusion criteria:
Chronic non-healing ulcers of 6 weeks duration.
Age >18yrs
Those willing to give consent

Exclusion criteria:
<18yrs age
H/o bleeding disorders, anaemia and other haematological disorders, platelet count <1.5lakh/cu.mm.
Patients on anticoagulant therapy (aspirin, warfarin, heparin), pregnancy and lactation, uncontrolled diabetes
Those not willing to give consent.

Procedure:
Patients were thoroughly examined and ulcer size (length, breadth and depth) was measured. Venous Colour Doppler was carried out for all patients. 2 patients had perforator incompetency and 1 patient had superficial vein incompetency.

Under aseptic precautions 10 ml of venous blood was drawn and added to a test tube containing acid citrate dextrose in a ratio of 9:1 (blood: Acid citrate dextrose), centrifuged at 1500 rpm for 15 min to separate the red blood cells from the platelets and plasma. Then the supernatant and the buffy coat composed of platelets and plasma was collected and centrifuged again at 3000 rpm for another 15 min. The bottom layer about 1.5 ml was taken and 10% calcium chloride was added (0.3 ml for 1 ml of PRP). The mean platelet count was 3.8 Lakhs/cumm (SD 0.95) and the mean final concentration of platelets in PRP was 6.05 Lakhs/cumm (SD 1.25). Thus the activated PRP was injected over the ulcer edges. The remaining PRP, if any, was applied onto the wound after proper surgical debridement and was dressed with a non-absorbent dressing (paraffin gauze). This process was repeated once weekly for 6 weeks. At every week the ulcer area and volume was calculated and photographs were taken. Wound area was calculated using the formula for an ellipse: Length × width × 0.7854 (an ellipse is closer to a wound shape than a square or rectangle that would be described by simple length × width). The use of an ellipse for calculating wound measurement has been used in RCTs in wound healing literature. Volume was calculated using the formula (length × width × 0.7854) × depth.

The treatment outcome was defined as a percentage change of the area and volume, which was calculated as initial measurement minus assessment day measurement divided by initial measurement.

It is basically based on utilizing the growth factors (such as vascular and endothelial) inflammatory and phagocytic (ILN4, ILN6, alpha tumour necrosis factor, etc.,) and antimicrobial properties of PRP for enhancing wound healing in a natural way and assisting the regeneration of skin from the margins. It is developed with the intention of keeping it reproducible at all level of health care including primary, which can be imparted by any trained physician, who have accessibility to a low rpm centrifuge machine, which in Indian market costs only Rs. 25,000-35,000.

PRP is a volume of autologous plasma that has a platelet concentration above baseline i.e., five times more than normal platelet counts.

PRP enhances wound healing by promoting the healing process by seven growth factors present in it. They are platelet derived growth factor (αα, αβ, αβ), 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 extra-cellular matrix synthesis during the healing process.

Chronic venous leg ulcers come with cost and morbidity for patients and society also. PRP is a safe, simple, inexpensive and biocompatible procedure. In our study, PRP is found to be useful in enhancing the wound healing in chronic venous leg ulcers without any adverse events.

Growth factors in Platelet Rich Plasma:
The important growth factors in PRP are :
Transforming growth factor-B - stimulates undifferentiated mesenchymal cell proliferation, endothelial chemotaxis, and angiogenesis, inhibits macrophage and lymphocyte proliferation, regulates endothelial, fibroblastic, and osteoblastic mitogenesis, mitogenic effects of other growth factors, collagen synthesis, and collagenase secretion
Platelet-derived growth factors (PDGF-AB and PDGF-BB) - mitogenetic for mesenchymal cells and osteoblasts, stimulates chemotaxis and mitogenesis in fibroblast, glial, or smooth muscle cells, regulates collagenase secretion and collagen synthesis, stimulates macrophage and neutrophil chemotaxis
Insulin-like growth factor (IGF) improves the early healing of tendon defects by over-expression of IGF-1, chemotactic for fibroblasts and stimulates protein synthesis, enhances bone formation

Vascular endothelial growth factors - stimulating new blood vessel formation to bring nutrients and progenitor cells to the injury site, stimulates mitogenesis for endothelial cells
Epidermal growth factor - stimulates endothelial chemotaxis or angiogenesis, regulates collagenase secretion, stimulates epithelial, or mesenchymal mitogenesis
Fibroblast growth factor-2 - stimulating new blood vessel formation to bring nutrients and progenitor cells to the injury site
Platelet factor 4 - stimulate the initial influx of neutrophils into wounds, chemoattractant for fibroblasts
Interleukin 8 - pro-inflammatory mediator, recruitment of inflammatory cells
Keratinocyte growth factor - promote endothelial cell growth, migration, adhesion and survival, angiogenesis.

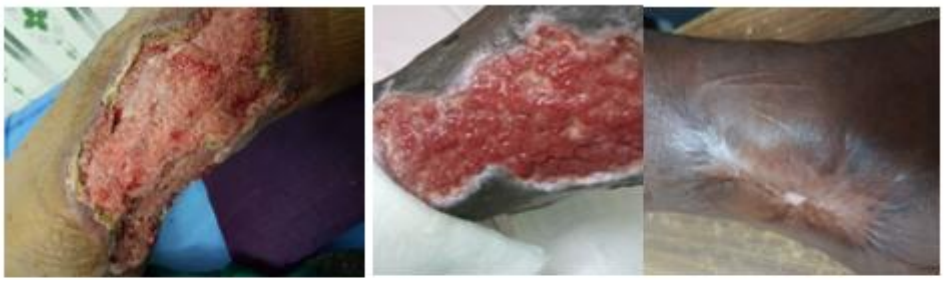
How they help:
Stabilize the damaged tissue during initial stages of tissue repair
Direct the local mesenchymal and epithelial cells to migrate, divide, and increase collagen and matrix synthesis
Ultimately leading to fibrous connective tissue and scar formation.

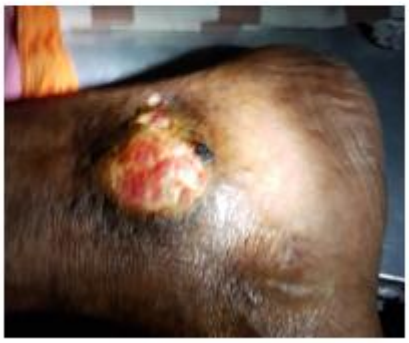
III. Results:

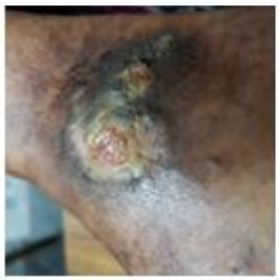
Sixteen patients were prospectively included in the study and were given PRP infiltration according to above protocol. The mean age of patients was 48.7 and average PRP infiltrations required were 9. All wounds showed encouraging signs of healing and healed almost completely. The wound healing was achieved in patients with diabetes with non healing ulcer, a case of Hansen's disease with non healing trophic ulcer, other causes like venous stasis etc. Excellent wound coverage was observed in these patients by the above procedure.

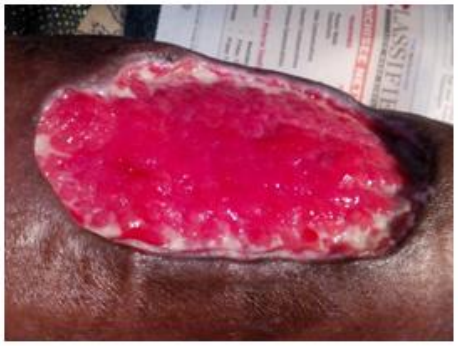
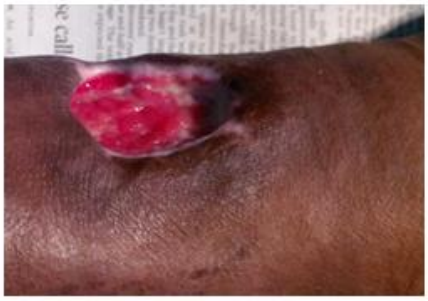
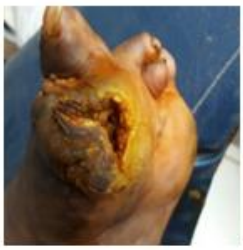
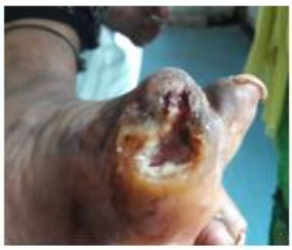
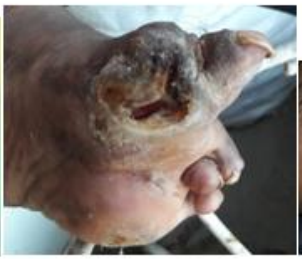
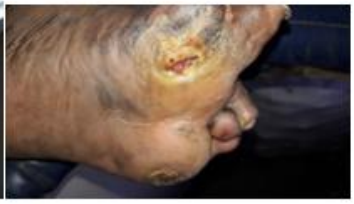
IV. Conclusion:

PRP is very promising futuristic therapy. It is a vehicle to deliver large amount of important growth factors, which are biologically active, to the injury site. Its use has increased extensively over the last decade due to advanced technology, availability of newer commercial PRP equipment, manufacturing various PRP products in the market. It is very simple and easy to use, easily available, uses patient own blood (autologous), potential cost-effective, and considered very safe therapy. There are many case series showing positive outcomes. But despite the promising results of several animal studies, well-controlled human studies are lacking. The research is still in its infancy. There is no consensus or protocol for the use of PRP. Even with all the limited evidence available, today PRP is becoming a very popular therapy in various fields of medicine. More research in future will clear the clouds over many questions being raised about the efficacy and evidence for PRP. To conclude, we may say that there are reasonable amount of data which warrant continued research in PRP but currently its role in clinical practice is not completely defined.







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