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Efficacy of Autologous Platelet Rich Plasma (PRP) Marginal Injections AndPRP Dressings in Large Chronic Wounds–A Prospective Observational Study

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Abstract

Background: Platelet-rich plasma (PRP) is one of the new modalities for treatment of acute and chronic wounds. Autologous PRP gel consists of cytokines, growth factors (GFs), chemokines, and fibrin derived from the patient's blood. The use of PRP is a safe, easy, and cost-effective method with better outcome in the management of chronic wounds. **Aim & Objectives:** To evaluate the efficacy of PRP dressings combined with marginal injections of PRP in large chronic wounds at different intervals after such dressings and to achieve wound healing in large chronic wounds which are otherwise very difficult to heal with routine dressing. **Methods**: The study was conducted on 25 patients of either sex, admitted for treatment of large chronic wounds in Orthopaedics Department, Guru Nanak Dev Hospital, Govt. Medical College, Amritsar. Three PRP dressings combined with marginal injection of PRP were given on day 0, after first week, and after 3rd week. On 2nd week, and 4th, 5th, 6th and 8th week, only saline dressings were applied at weekly intervals. On each dressing, patient's wound was measured in length and breadth by using a scale and area was calculated. The %age of wound closure was also estimated. The data was tabulated and subjected to statistical analysis. **Results**: We found that 88% cases showed excellent results and 12% cases showed good results. There was significant difference in length, breadth, area of wound and %age of wound closure at different intervals ($P< 0.05$). **Conclusion**: Autologous platelet rich plasma dressing is an effective method to enhance healing in large chronic wounds/ulcers. However, further research and controlled, randomized prospective clinical trials with larger sample size are required to validate the results.

Keywords: Chronic Wounds, Autologous, PRP, Marginal Injection

INTRODUCTION

Wounds are classified as acute or chronic according to the persisting duration, however, there is no specific length of time to define chronicity.[1] Chronic wounds are defined as wounds, which have failed to proceed through a timely and organized reparative process to produce

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anatomic and functional integrity. These wounds are deficient in the growth factors required for healing, they are often difficult to heal and may be associated with super added infection.[2]

The prevalence of chronic non healing ulcer in the world ranges from 1.9 to 13.1%. The incidence of chronic ulcers is expected to increase with the increasing age and presence of risk factors for atherosclerotic occlusion such as smoking, obesity and diabetes. It is estimated that almost 10% of the population would develop a chronic wound in the course of a lifetime; with wound related mortality rate of 2.5%.[3] The standard available treatment modalities provide optimal local ulcer therapy with debridement of necrotic tissue and provision of a moist wound healing environment, pressure relief in the wound area, infection management using antibiotics, antiseptics and topical antibacterial agents, management of ischaemia and comorbidities. The methods generally used for management are hyperbaric oxygen therapy, maggot therapy and negative pressure wound therapy.[4] Platelet-rich plasma (PRP) is a newer method of wound therapy for acute and chronic wounds. Autologous PRP gel consists of cytokines, growth factors (GFs), chemokines, and fibrin derived from the patient's own blood. The mechanism of action for the PRP gel is thought to be the induction of normal wound healing responses at molecular and cellular levels. Autologous PRP is a safe, easy, and cost-effective method with good promising results in the management of chronic non-healing ulcers.[5,6]

Since chronic wound patients demonstrate deficiency of biological stimulators, PRP can enhance the healing process. This study was planned to achieve wound healing in large chronic wounds which were otherwise very difficult to heal with routine dressing and to evaluate the efficacy of PRP dressings combined with marginal injections of PRP in large chronic wounds at different intervals.

MATERIALS & METHODS

The study was conducted in the Orthopaedics Department, Guru Nanak Dev Hospital, attached to Govt. Medical College, Amritsar on 25 patients of either sex admitted for treatment of large chronic wounds. The written informed consent of each patient was taken before the study. Approval from institutional ethics committee was also taken.

Exclusion Criteria:

- Patients with liver cell failure.
- Patients with severe cardiomyopathy.
- Patients with major lower limb amputation.
- Patients with bleeding or platelet disorder.
- Patients with low immunity or corticosteroid therapy.

Wound size as per maximum length and breadth and area was recorded and three PRP dressings combined

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with marginal injection of PRP were given. First on day 0, second after first week, and third after 3rd week. On 2nd week, and 4th, 5th, 6th and 8th week only saline dressings were applied at weekly intervals. On every dressing patient's wound was measured in maximum length and maximum breadth by using a scale and area was calculated.

Preparation of Autologus Platelet Rich Plasma:

A triple blood bag was taken, and 48 ml of CPD (citrate phosphate dextrose) was removed and discarded which left just 14 ml of CPD in the bag. 100 ml of patient's whole blood was drawn by a clean, single venipuncture, into the 1st blood bag. The bag was kept at room temperature (20-22 degrees C) before preparing platelet concentrate for not more than 6 hours. The bag was kept in the bucket of refrigerated centrifuge (Heraeus Cryofuge 6000i) and balanced accurately, and centrifuged at 2000 rpm at 22 degrees C for 5 minutes. This separated the whole blood into red blood cell concentrate at the bottom and plasma above.

4/5th of the plasma was separated into the 2nd satellite bag and the tubing was double sealed between the primary bag and the satellite bag. The primary bag with RBC concentrate was separated and kept aside. The remaining 2 satellite bags were again centrifuged at 4000 rpm at 22 degrees C for 10 minutes after accurate balancing. The plasma was separated into an upper layer of platelet poor plasma (PPP) and platelet concentrate (PRP) below. The PPP layer was expressed into the 2nd satellite bag, double sealed, separated and kept aside.

The PRP (platelet concentrate) extract in the 1st satellite bag was approximately 12- 15 ml. This bag was sent to the operation theatre immediately, where it was kept at room temperature before use.

Prp dressing and marginal injection procedure:

PRP was removed from blood bag using aseptic technique and was put in a sterile container. Wound was cleaned with normal saline and scrapped & pressed to achieve control of bleeding if any. Then sterile gauze was soaked in PRP and applied over the wound area & marginal injection of 1ml PRP at one inch intervals was given. Patient was advised to walk with partial weight bearing. Dressing was opened after one week when similar dressing and marginal injection of 1ml PRP at 1 inch interval were given again. Then one week later simple normal saline dressing was done & one week later 3rd PRP Dressing and marginal injection of 1ml PRP at one inch interval were given. Then at weekly interval normal saline dressings were done. At every dressing, area of the wound was measured by taking maximum length and breadth &if there is any change it was recorded.

RESULTS

In each patient area was calculated as per maximum length and maximum

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breadth till maximum 8th week. Results were evaluated as area of closure of wound. In many cases there may be earlier healing of wound, so they were evaluated upto that time only. Complication if any was recorded and managed appropriately. The results were graded according to following criteria:

Grading of results	
90-100% healed	Excellent
70-90% healed	Good
50-70% healed	Fair
Less than 50% healed	Poor

Appropriate statistical tests were applied for results.

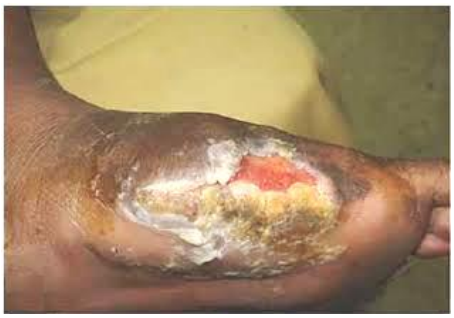

Figure 1: At Day 0 (1st Prp Dressing and Marginal Injection)

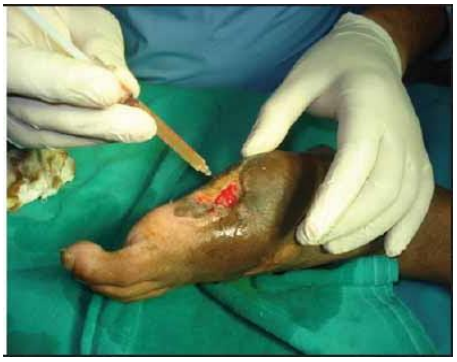

Figure 2: After One Week (2nd Prp Dressing and Marginal Injection)

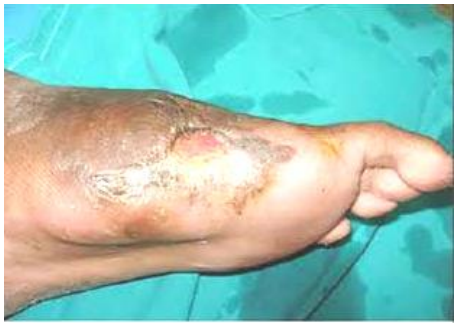

Figure 3: After Two Weeks (Ns Dressing Applied)

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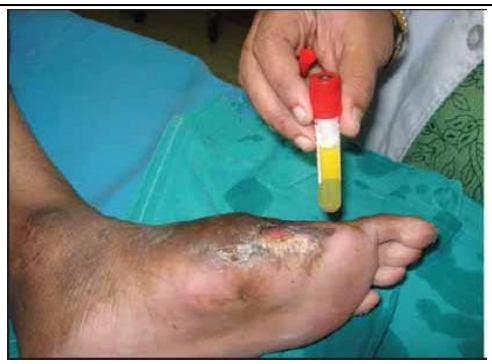

Figure 4: After 3 Weeks (3rd Prp Dressing and Marginal Injection)

Figure 5: After 4 Weeks (Ns Dressing Applied)

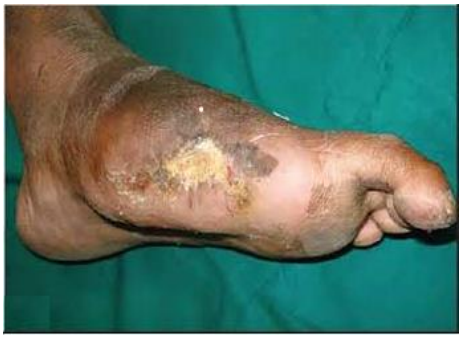

Figure 6: After 5 Weeks (Ns Dressing Applied)

The study population comprised of 56% males and 44% females. Majority of patients (48%) were in age group 50-70 years, followed by 30-50 years (40%) and least in age group 70-90 years (12%). Maximum wounds (68%) were 6-9 weeks old, 28% were 10-12 weeks old whereas 4% were >12 weeks old.

We found that 68% wounds took 6-8 weeks to heal, 24% took greater than 8 weeks to heal and 8% wounds took 4-6 weeks.

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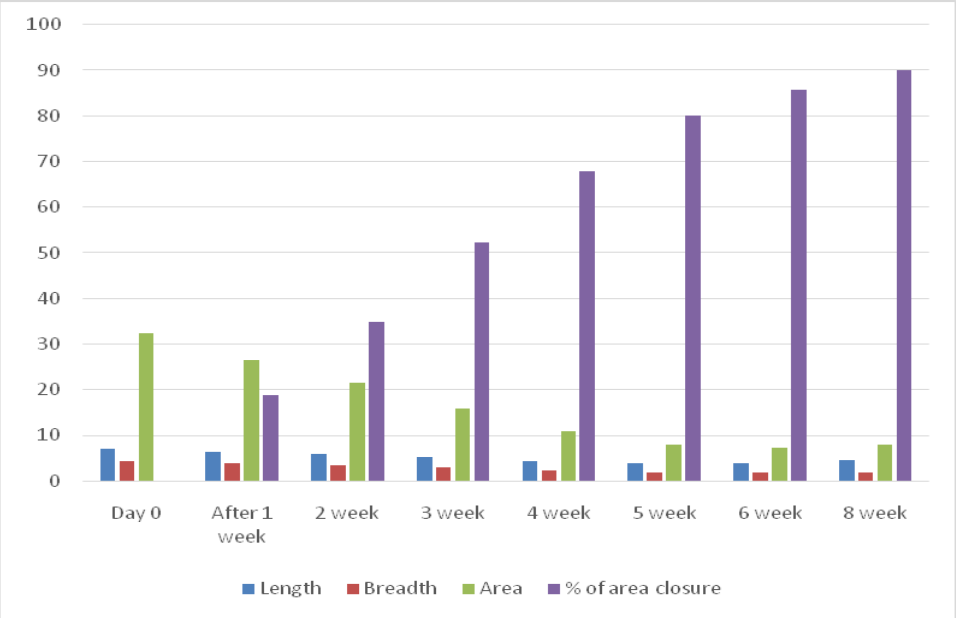
Parameters	Day 0	After 1 week	2 week	3 week	4 week	5 week	6 week	8 week	P value
Length	7.06	6.42	5.84	5.1	4.34	3.87	3.8	4.5	0.000
Breadth	4.38	3.9	3.48	2.94	2.34	1.79	1.7	1.75	0.000
Area of wound	32.3	26.36	21.48	15.83	10.89	7.87	7.28	7.94	0.000
% of wound closure	0	18.77	34.80	52.36	67.94	80	85.70	89.94	0.001

Table 1: Comparison at Day 0 and Following Weeks



Graph 1: Comparison at Day 0 and Following Weeks

We observed significant difference in wound dimensions- length, breadth, area of wound and percentage of wound closure at day 0, after 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks, 6 weeks and 8 weeks($p<0.05$).

88% cases showed excellent results and 12% cases showed good results. This was found to be statistically significant ($p< 0.05$).

DISCUSSION

In 1986, Knighton et al[7] showed that the use of autologous platelet factors accelerated epithelialisation of granulation tissue leading to complete repair of chronic non-healing ulcers. Frykberg et al[8] conducted a study on 49 patients with 65 non-healing ulcers out of which 63 ulcers responded with a reduction in area, volume and undermining of the ulcers in a mean duration of 2.8 weeks with 3.2 treatments. Another study by Kakudoet al,[9] treated five cases of intractable skin ulcer with autologous PRP, among which three ulcers healed completely within 4 weeks and epithelialiazation of wound occurred within 6.6 weeks on average. Steenvoorde et al[10] conducted a study

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on 12 patients with 13 wounds where seven of 13 wounds required more than one application, with a mean number of 2.2 applications and a mean treatment period of 4.2 weeks.

Our results were consistent with the study done by Suthar M et al[4] on 24 patients where one wound/ulcer per patient was treated with a single dose of a combination of autologous PRP gel and subcutaneous injections of PRP in and around the wound periphery. Each patient showed wound healing with reduction in wound dimensions, and the mean time taken for healing of the ulcers was 8.2 ± 1.9 weeks. Our results were also in accordance with the study done by Asif et al,[2] which showed that APRP application had faster and better healing rates with good percentage reduction of ulcer area. There were no adverse effects or reactions seen with use of APRP.

Liu H et al found that PRP makes significant changes in monocyte mediated release of proinflammatory cytokines/chemokines and ancreases the level of lipoxin A 4, thus limiting inflammation and infection.[11]

PRP treatment is painless which isbetter tolerated by the patients. Safety is another benefit of PRP treatment as it uses the patient's own blood. It avoids risk of viral infections such as HIV, hepatitis, West Nile fever, and Creutzfeldt–Jakob disease. It is also free from concerns over antibody formation and risk of graft-versus-host disease, which together lead to better acceptance by patients. It is also less invasive and more economical compared to other novel therapies. However, there are limitations regarding PRP treatment. The main limitation is that only a limited number of clinicians are currently able to use PRP treatment because of facility limitations and lack of uniform protocol. In addition, evidence on PRP's effectiveness is not yet fully established. Another concern is the quality of the end product which may vary with working procedures of blood establishments. Viability and quantity of cytokines in platelets are reported to decrease, especially in patients with diabetes, so PRP treatment may not be as effective as expected in certain patients.[12]

CONCLUSION

Chronic wounds are a growing socioeconomic concern all over the world. The conventional treatment modalities available for chronic wound healing are time consuming and expensive. Autologous platelet rich plasma dressing is a safe and cost-effective method. The usage of PRP in treatment of chronic wounds/ulcers not only enhances healing, but also prevents lower extremity amputations caused by non-healing wounds. Furthermore, no special considerations are required regarding antibody formation and the risk of graft vs. host disease which leads to better acceptance by patients. However, advanced research and controlled, randomized prospective clinical trials on larger patient population are necessary to validate the results.

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