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Original Research Article

Efficacy of autologous platelet rich plasma versus regular dressing in chronic wounds

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ABSTRACT

Background: Chronic wounds are a frequent problem and pose a heavy burden to the service provider. Platelet extract containing several growth factors used on chronic wounds has shown impressive results in both healing percentage and time for epithelisation. Platelet extract from the patient's own blood has been used in trials as a cheap and equally effective alternative to commercial platelet gels. The aim of the study was to demonstrate the therapeutic role of autologous platelet rich plasma (APRP) in epithelialisation and reduction in size of chronic wounds of lower limb.
Methods: It is a case control study, conducted at Sri Adichunchanagiri Hospital and Research Centre, B.G. Nagara, Karnataka. Conducted during January 2017 to June 2018 this study consisted of 30 patients with chronic ulcers between the age group of 18-80 years, with duration of ulcer ranging from 12 to 26 weeks. After obtaining consent they were randomly allotted into control and test groups with 15 patients each. Control group patients were treated with conventional dressing and in test group APRP dressing was done. Later percentage decrease in wound size was assessed.
Results: Ulcer size decreased significantly ($p<0.0001$) in test group compared to control group. No unwanted effects or complications noted.
Conclusions: APRP is a safe and effective treatment modality for chronic non-healing ulcers. It enhances healing and also decreases the associated cost and morbidity. Further research and randomized controlled clinical trials on larger patient population are necessary to validate the results.

Keywords: Autologous platelet rich plasma, Chronic wounds, Ulcer healing

INTRODUCTION

Chronic wounds are a major health challenge. The goal of wound care in chronic ulcers is to facilitate healing using standardized protocols of wound care.

A practical classification of a non-healing wound is one that fails to heal spontaneously within 3 months.[1]

Apart from the conventional methods to facilitate wound healing various new methods are emerging such as cellular therapies which include platelet-rich plasma (PRP) and collagen based wound dressing. This can have an adjunctive role in a standardized, quality treatment plan.[2,3] Platelets release certain growth factors from alpha granules which are located in thrombocyte cell membrane which include platelet derived growth factor (PDGF), epidermal growth factor (EGF) and platelet derived angiogenesis factor which act locally and hasten the healing process. Platelet extract has been used in many studies and has shown impressive results in healing of chronic non healing ulcers.

Since not all patients can afford commercially available recombinant platelet gel for dressing, platelet extract from the patient's own blood/allogenic platelet concentrate available has been used in trials on chronic wounds.

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 as the population ages and due to increased 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%.[4]

The purpose of this study is to evaluate how autologous platelet rich plasma (APRP) affects wound healing of chronic non-healing wounds in a hospital care setting.

METHODS

This is a prospective case-control study with simple randomisation. After obtaining approval from ethical committee, the present study was conducted from January 2017 to June 2018 on 30 patients (sample size) of Chronic non healing ulcer attending surgery OPD at Sri Adichunchanagiri Hospital and Research Centre, B.G. Nagara.

Patients included were in the age group of 18 to 80 years with chronic long standing non-healing neuropathic ulcers of lower limb. Duration of ulcer was 12 to 26 weeks**.** All patients had clinically no abnormality in vascularity to the ulcer area.

Ischemic ulcers, ulcers with evidence of malignancy, active infection with pus discharge, slough, evidence of gangrene in the ulcer or on any other part of limb and patients currently receiving or has received radiation or chemotherapy within the last 3 months were excluded from the study.

After obtaining permission from institutional ethics committee, about 100 patients were assessed for eligibility of which about 70 where excluded due to not meeting inclusion criteria and not willing for participation. Two groups were randomly assigned as the cases A (test group, n=15) and controls B (control group, n=15).

The method of study consisted of consent to investigate and treat as a part of the study, detailed history taking & thorough clinical examination as per the structured proforma. Routine blood investigations and viral markers were tested. Glycemic status assessed and controlled (Through the entire treatment period normoglycemia was maintained - fasting blood sugar ≤110 mg% and Post-prandial blood sugar ≤140 mg%).

Patients were included after correcting anemia and hypoalbuminemia (baseline hemoglobin more than 10 gm% and Serum albumin more than 3 gm%). Size of the wound was assessed by placing a meter scale from the edges of the wound in their longest dimensions (length, breadth and depth). Initial areas varied from 9 to 12 cm^2 (approximated). Fibrous margin was removed initially. APRP or conventional dressing was done as per their groups after randomizing the patients.

Technique for conventional dressing

The ulcer was cleaned with 0.9% saline solution and was covered with a pad and roller bandage.

Technique for APRP dressings

20 ml blood was collected from the patient and platelet rich plasma was freshly prepared using centrifugation. Then it was applied during each dressing after cleaning with 0.9% saline and dressing done using pad and roller bandage. Maximum of 5 ml of PRP was used in one sitting and it was used uniformly over the ulcer and the procedure was done on OPD basis and in wards. The dressing was changed every 4th day in both the groups.

The end point of the study was taken as the area of wound contraction at end of 4 dressings, complete closure or end of follow up. Size of the wound was assessed after this period. Mean, difference in means and statistical significance was calculated using MEDCALC® statistical software.

RESULTS

In this study end result was established by calculating the percentage area of wound reduction after 4 dressings or completes epithelisation of the wound within this time period.

A total of 30 patients were studied, with overall age range from 18 to 80 years. Age ranged from 29 to 80 years in the test group (A) and 18 to 79 years in the control group (B). Age wise division of patients in both groups is compared in Table 1.

Table 1: Age ranges compared among test and control groups.

Age range (years)	No of patients in test group	No of patients in control group
<30	1	2
30 - 50	3	4
50 - 70	6	5
>70	5	4

Duration of wound ranged from 12 to 26 weeks. The wound duration comparison between the two groups is depicted in Table 2.

Table 2: Duration of wounds compared among test and control groups.

Duration of wound (in weeks)	No of patients in test group	No of patients in control group
12-16	4	4
17-21	6	5
22-26	5	6

Initial wound sizes ranged from 9 to 12 cm^2 in both the groups. The initial and final wound sizes and percentage reduction in wound sizes is compared between the two groups in Table 3.

Wound reduction in the groups was as high as 100% (complete epithelisation) as seen in group A and as low as 11.11% as noted in group B. The patient in group A with complete epithelisation of the wound within 4 dressings, was a 59 yr old male patient with ulcer duration of 23 weeks and had an initial area of about 12 cm^2. Despite older age and bigger surface area because of APRP dressings he had complete wound healing.

Table 3: Wound sizes compared among test and control groups (before and after treatment).

Patient no.	Test group (A)			Control group (B)		
	Initial area (cm^2)	Final area (cm^2)	% of area reduced	Initial area (cm^2)	Final area (cm^2)	% of area reduced
1.	9	2	77.77	9	7	22.22
2.	9	3	66.66	9	7	22.22
3.	9	1	88.88	9	8	11.11
4.	9	2	77.77	9	7	22.22
5.	9	2.4	73.33	9	6	33.33
6.	9	2	77.77	10	8	20
7.	9	2	77.77	10	8	20
8.	11.25	3	73.33	10	8	20
9.	12	1	91.66	10	7	30
10.	12	3	75	12	7.5	37.5
11.	12	2	83.33	12	9	25
12.	12	0.75	93.75	12	9	25
13.	12	0	100	12	9	25
14.	12	2	83.33	12	9	25
15.	12	2	83.33	12	9	25

The mean reduction in test group (A) where APRP dressings were done was 81.58% and that in control group (B) with conventional dressings was 24.24%.

Difference in means was 57.340. Standard error was 2.798. 95% CI was 51.6079 to 63.0721, t-statistic was 20.491 and Significance level $p<0.0001$.

DISCUSSION

Chronic wounds are a major health problem especially in developing countries like India, and these wounds lack the necessary growth factors for healing, they are often difficult to heal and are associated with super added infection. Chronic wounds are defined as wounds, which have failed to proceed through an orderly and timely reparative process to produce anatomic and functional integrity.

The main goal of any treatment modality is to obtain wound closure expeditiously.

The conventional treatment includes adequate debridement, control of infection, revascularisation 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.

No significant difference in healing rates was found while comparing different types of dressings, beneath appropriate compression bandages in a Cochrane study, where the authors compared hydrocolloids, foam dressings, alginates, low-adherent dressings, and hydro-gels.[5] Topical application of epidermal growth factor (EGF) to non-healing ulcers did not promote re-epithelialization.[6]

Topical silver or silver dressings are used in infected wounds of all origins, but evidence for their efficacy is lacking.[7] An experimental tool used in combination with standard wound care, topically applied working platelet rich plasma (PRP), may be used to boost chronic inflammatory wounds into the state of proliferation and healing as they release multiple growth factors and cytokines into the wound mimicking natural healing conditions.[8,9]

Presently as for pressure ulcers, standard treatment consists of pressure relief, surgical debridement and maintenance of a clean wound environment along with

systemic antibiotics. Dressings containing antimicrobial or pain relieving substances used beneath compression bandages are currently being developed.[10]

PRP contains various necessary growth factors for wound healing. In addition, the high concentration of WBC's present in PRP is also helpful in preventing infections and platelet rich plasma has already been used to treat wounds since 1985.[11,12]

A prospective, randomized, controlled, blinded multicenter study conducted by Driver et al, initially included 72 patients with diabetic foot ulcers who were treated with autologous platelet-rich plasma gel or control (saline gel). However, 32 patients were excluded from the final protocol because of protocol violations and failure to complete treatment. Their study results showed that significantly more wounds healed in patients treated with platelet-rich plasma gel (13 out of 16 or 81.3%) than patients treated with control gel (eight out of 19 or 42.1%). However, the study had several limitations including small sample size, protocol violations occurring during the study period, and high rate of patient dropouts.[13]

A recent meta-analysis of the use of APRP therapy in cutaneous wounds showed that compared to control wound care, APRP facilitates wound healing and the ulcers improved significantly in small hard to-heal acute and chronic wounds.[8,14] In addition, platelets exert antimicrobial activity against some bacteria of the skin, and clinical data shows that the presence of infection is reduced in APRP treated wounds.[14] Therefore, APRP therapy has several advantages that can provide a practical and effective treatment approach for small hard-to-heal ulcers.[15]

Hence, the present study was done to demonstrate the therapeutic role of APRP in healing of chronic non-healing ulcers where better healing rates were established with use of PRP in chronic non healing ulcers. The baseline characteristics such as age, sex and location of the ulcer were similar in the patients who received PRP dressing in study group and in patients who received control dressing.

In 1986, Knighton et al showed that the use of autologous platelet factors accelerated epithelialisation of granulation tissue leading to complete repair of chronic non-healing ulcers. This was the first clinical study that demonstrated the promising role of locally acting factors derived from autologous blood in promoting healing of chronic cutaneous ulcers.[16]

The growth factors released from PRP are important in modulating mesenchymal cell recruitment, proliferation and extracellular matrix synthesis during the healing process.[17]

The mechanism of action for PRP is thought to be the molecular and cellular induction of normal wound healing response similar to that seen with platelet activation.[18] PRP accelerate all phases of wound healing (most prominent in angiogenesis).[18]

In the present study, initial area of the ulcer (in cm^2) was similar between the two groups. However, the final wound size, overall time and number of dressing required for complete closure was significantly less in those treated with PRP as compared to the control group and this difference was statistically significant.

A study conducted by Frykberg et al on 49 patients with 65 non healing ulcers showed that 63 of 65 ulcers responded with a reduction in area, volume of the ulcers in a mean duration of 2.8 weeks with 3.2 treatments.[19] Steenvoorde et al conducted a study on 12 patients with 13 wounds, showing that 7 of 13 wounds required more than 1 application, with a mean number of 2.2 applications and a mean treatment period of 4.2 weeks.[20]

Kakudo et al treated five cases of intractable skin ulcer with autologous PRP, among which three ulcers healed completely within 4 weeks and epithelization of wound occurred within 6.6 weeks on average.[21]

Till now there is no standard method of preparation of PRP in literature. According to Marx, the device must use a double centrifugation technique.[22] Regardless of the rate of centrifugation or the time of centrifugation, a single spin cannot adequately concentrate platelets, because the red blood cells will interfere with their fine separation.

Several studies have been conducted on the use of PRP for the treatment of non-healing ulcers and the results have been promising, however, currently, there is a paucity of critical scientific data regarding the beneficial effects of APRP in clinical procedures. That is the inspiration in doing the present study, so as to provide what all clinical supportive data is necessary, even in smaller amounts to further substantiate the usefulness of APRP over traditional dressings in chronic non healing wounds.

CONCLUSION

Chronic wounds/ non-healing ulcers are a growing socioeconomic problem all over the world. All the conventional treatments relating to chronic wound healing/ulcer is time consuming and expensive. Autologous platelet rich plasma dressing might prove the first line remedy for the same and should be promoted as it is safe and cost- effective.

In this study 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.

This way of treatment has been mentioned in literature as well as used by few clinicians and hereby, we are

strengthening their view with these cases as this might become the first treatment of choice in non-healing wound/ulcer.

The results from this case series showed that APRP is a safe and effective treatment modality for chronic non-healing ulcers. Using APRP to treat chronic wounds/ulcers may not only enhance healing, but also prevent lower extremity amputations caused by non-healing wounds. Therefore, further research and randomized controlled clinical trials on larger patient population are necessary to validate the results.

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