ORIGINAL RESEARCH PAPER

Dermatology

AUTOLOGOUS PLATELET RICH FIBRIN MATRIX (PRFM): IN TREATMENT OF CHRONIC NON-HEALING ULCER

KEY WORDS: Autologous platelet-rich fibrin matrix, Chronic non healing ulcer, Growth factors.

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ABSTRACT

BACKGROUND: Patients with chronic non-healing ulcer of various etiology are one of the major causes for disability. It has been shown that autologous platelet-rich fibrin matrix (PRFM) is effective in the healing of chronic non-healing ulcer, especially on lower-limb. **AIM:** This is prospective interventional study to demonstrate the efficacy of autologous PRFM in chronic non-healing ulcer. **METHODS:** This is prospective study conducted in total 25 patients having non-healing ulcer due to various etiology of more than 6 weeks duration, were treated with PRFM, repeated once a week until complete re-epithelisation occurred or maximum of 6 sittings as per requirements. Clinical photographs were taken and area of ulcer was calculated at every follow up. **RESULTS:** Out of total 25 patients with chronic non-healing ulcer over lower limbs, 9 ulcers were due to leprosy, 3 ulcers were venous ulcer, 2 ulcers were due to alcoholic neuropathy and 11 ulcers were due to diabetes mellitus. The mean duration of healing of ulcer was 3.96 weeks. The mean of area and volume at the end of 5th sitting was 0.32cm2 and .001cm3. **CONCLUSION:** Autologous platelet-rich fibrin matrix for the treatment of chronic non-healing ulcers is safe, simple, effective and inexpensive therapy without any complication and side effect.

INTRODUCTION:

Chronic non-healing ulcers are defined as spontaneous or traumatic lesions, that are unresponsive to initial therapy or that persist despite appropriate care and do not heal in a defined time period with an underlying aetiology that may be related to systemic disease or local disorders [1,2].

Causes of chronic non healing ulcer are chronic venous disease, peripheral vascular disease, Hansen's disease, diabetes, trophic ulcer and traumatic. Healing of an ulcer occurs in three stages: inflammation, tissue regeneration and tissue remodelling. If the normal healing of an ulcer is interrupted at any stage by above mentioned cause or any unknown reason, it may convert into chronic ulcer or nonhealing ulcer. Most of the time it is due to lack of growth factors and cytokines which delay the healing process [3]. Lower extremity is the most common site for chronic non healing ulcer attributed to venous disease, arterial disease or diabetes.

Prevalence of non-healing ulcer in the world ranges from 1.9%-13.1% [4,5]. In India, it is 4.5 per 1000 population as estimated by Shukla et al [6]. The incidence of non-healing ulcer is expected to increase as risk factors in person's life like smoking, obesity, diabetes, age etc. increases. It is estimated that almost 10% of the population would develop chronic ulcer in the course of the lifetime and wound related mortality rate is estimated to be 2.5% [7].

Conventional methods of treatment of nonhealing ulcers include wound cleaning, debridement, treatment of infection by antibiotics, antiseptics, topical antibacterial agents, maintenance of blood glucose level (in case of a diabetic patient), local care with dressing application [2,8,9]. Advanced methods for treatment of chronic ulcer includes skin grafting, hyperbaric oxygen therapy, vacuum assisted closure (VAC), angioplasty, reconstructive surgery [3,10,11].

Topical application of platelet derived growth factor (becalpermin) and epidermal growth factor are also considered under treatment modalities as lack of growth factor is one of the major causes of nonhealing ulcer. Recently, a newer modality of treatment named autologous PRFM (platelet rich fibrin matrix) came into picture which on topical application, delivers cytokines and growth factors to localized area and hasten wound healing. It is simple, safer, cheaper, less time-consuming procedure.

MATERIALS AND METHODS:

A prospective, non-randomised interventional trial was conducted on patients coming to G.K. General hospital, Bhuj with chronic non healing ulcer due to various causes from January 2019 to January 2020. In this study total 25 patients between the age group 18-70 years were included having total 28 non healing ulcers.

Inclusion criteria:

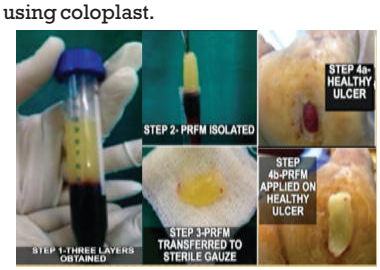
Patient with chronic non-healing ulcer persisting more than 6 weeks, Patient willing to participate in study and willing to give written informed consent, Patient above age of 18 years.

Exclusion criteria:

Patient less than 18 years of age, not willing to participate in the study or not willing to give informed consent, patients with bleeding disorders, on anticoagulants, thrombocytopenia, uncontrolled diabetes, active infection at the site, malignant ulcers, pregnant and lactating females.

METHODS:

Detailed history of patient including name, age, sex, occupation, address, use of medication was taken. Patient was thoroughly examined. Both general examination and local examination was done. Ulcer size in length, depth and width was measured. Routine investigation including CBC, HIV, HbsAg, was done. A written informed consent was taken. 10 ml of patient's venous blood was collected into plain vacutte (without anticoagulant) under strict aseptic precaution. After that, centrifugation was done at 3000 rpm for 7 minutes. After 7 minutes, a three-layered solution was obtained. The first layer or the upper layer was straw coloured PPP (platelet poor plasma) which was discarded. The second layer or the middle layer is PRFM and the bottom layer is red coloured containing RBCs. PRFM was separated from the bottom layer by using sterile forceps. PRFM was transferred to wound and dressing was done using coloplast.



This procedure was repeated every week for maximum up to 6 sittings. In every sitting, photographs of the ulcer were taken and healing was assessed by measurements of ulcer and volume of ulcer. Wound area was calculated using ellipse formula as ellipse is closer to a wound than a square or rectangle[12]. The formula for area of ellipse is (length* width*0.7854) and for volume, it is (area*depth).

RESULTS:

25 patients having non healing ulcer of various aetiologies described in table 1 were treated with PRFM at weekly intervals for maximum 6 settings. Out of the 25 patients 17 patients were MALE and 8 were FEMALE. The mean age of the patients was 40.48 years. The duration of the ulcer ranged from 1 months to 1 year. The mean duration of healing of ulcer was 3.96 weeks. The baseline mean area and volume of the ulcer was 9.32cm2 and 4.01cm3. The mean of area and volume at the end of 5th sitting was 0.32cm2 and .001cm3. Volume of ulcer improve faster than area. Ulcer due to Hansen's diseases healed faster than others. Treatment was completed within 40 minutes in all cases.

TABLE: 1 According to aetiology

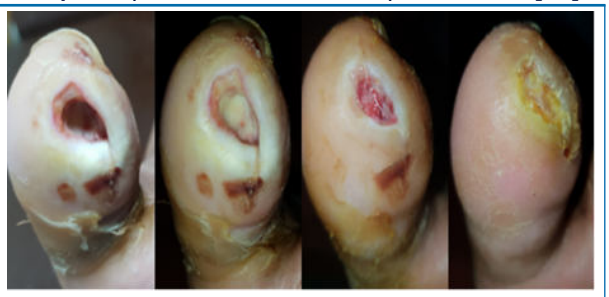
Cause of ulcer	No. Of ulcer
Leprosy	9(36%)
Venous ulcer	3(12%)
Alcoholic neuropathy	2(8%)
Diabetes mellitus	11(44%)
Total	25

TABLE:2 According to age and sex

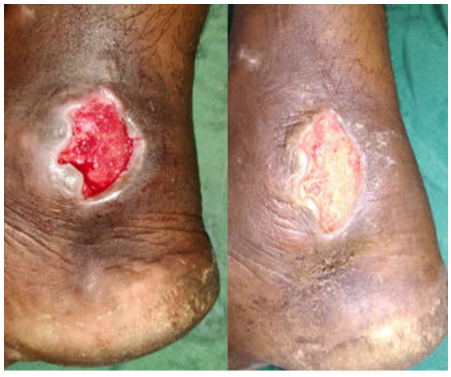
Age	Male	Female	No. of ulcers
21-40	10	5	15(60%)
41-60	5	3	8(32%)
>60	2	0	2(8%)
Total	17	8	25

TABLE:3 According to duration

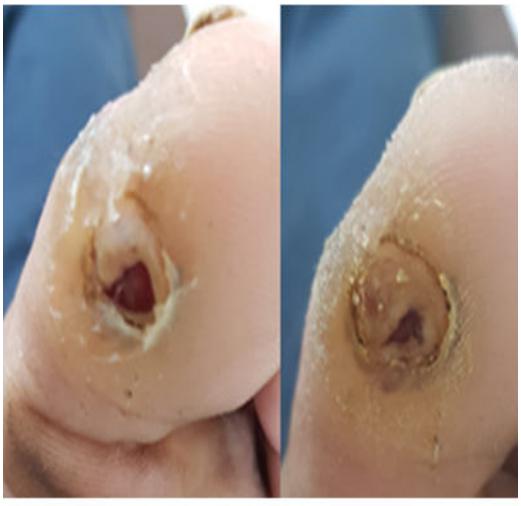
Duration of ulcer (in months)	No. of ulcers
<3months	15(60%)
3-6 months	7 (28%)
>6 months	3(12%)
Total	25



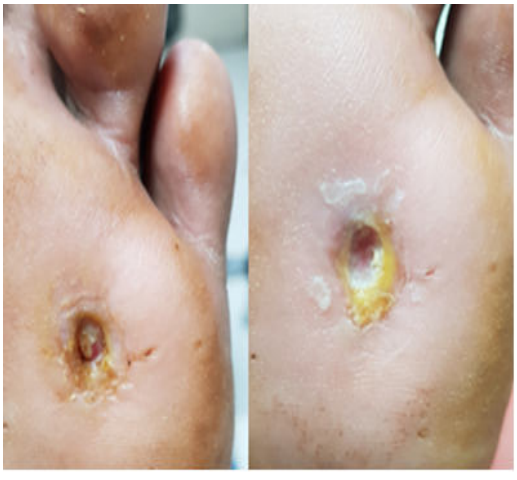
ULCER D/T DIABETES HEALED AFTER 4 PRFM



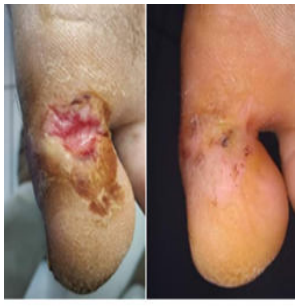
After 5th sitting of PRFM



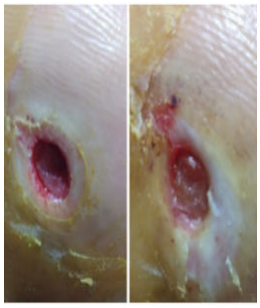
After 3rd sitting of PRFM



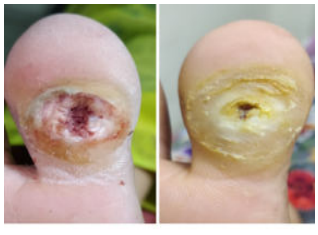
After 1st sitting of PRFM



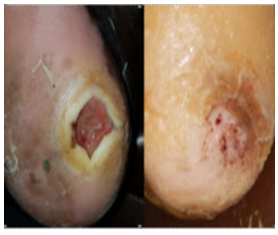
After 3rd sitting f PRFM



AFTER 1ST PRFM



After 2nd PRFM



After 4th sitting of PRFM

DISCUSSION:

Chronic non-healing ulcers are difficult to treat for a doctor. Various treatment modality for nonhealing ulcers are regular dressings, vacuum assisted closure, hyperbaric oxygen therapy, reconstructive surgery, surgical debridement etc. Topical platelet derived growth factors for treatment of chronic non-healing ulcers is an FDA approved modality but it is costly and unaffordable in developing country[13]. PRFM is an alternative to that and much cheaper, safe and easy procedure.

The first study that demonstrated the promising effect of locally acting growth factor was done in 1986 by Knighton et al.[14] Platelet contains large number of growth factor, cytokines, chemokines. They play main role in early stages of wound healing by contributing in inflammation and tissue repair. This characteristic of platelets leads to idea of using platelet as therapeutic tool for non-healing wounds[15,16]. Separating the platelets from blood and applying it on non-healing ulcer will move the ulcer out of inflammatory cycle into proliferative cycle by its anti-inflammatory property.

PRFM was first developed by Choukroun et al.[17]for use in oral and maxillofacial surgery. Making of PRFM is a simple procedure and does not require any anticoagulant. It can be obtained just by centrifugation of blood also known as Choukroun PRF. As there is no anticoagulants, platelets are not required to activated unlike PRP. Platelets get activated by coming in contact with tube walls and it starts the coagulation cascade and three layers re formed at the end of centrifugation: the RBC base layer, acellular plasma top layer and a PRF clot in the middle. Unlike PRP, the PRF does not dissolve quickly and a strong fibrin matrix is slowly remodelled in a similar way to a natural blood clot (Dohan et al. 2006).

A study done by Yazawa et al. (2003) showed that superior results can be obtained by PRF than PRP. It is because, when incorporated into drug delivery systems such as fibrin, the mean concentration of growth factors in the platelet concentrates was three times or more than that observed with conventional platelet-rich plasma. Growth factors from fibrin matrix released in slowly controlled manner over 1-week time and it was observed that it resulted in better healing of ulcer than PRP (Dohan et al. 2006).

CONCLUSION:

PRFM for the treatment of chronic non-healing ulcers is safe, simple, effective and inexpensive therapy without any complication and side effect. Limitation in this study is smaller sample size, thus most study with larger sample size are awaited to see long term efficacy and safety of PRFM in non-healing ulcers.

REFERENCES:

1. Sebastian KMS, Lobato I, Hernandez I, et al. Efficacy and safety of autologous platelet rich plasma for the treatment of vascular ulcers in primary care: phase III study. BMC Fam Pract. 2014;15:211.
2. Greer N, Foman N, Dorrian J, et al. Advanced wound care therapies for nonhealing diabetic, venous, and arterial ulcers: a systematic review. 2012. VAESP Project #09-009.
3. Martinez-Zapata MJ, Martí-Carvajal AJ, Solà I, et al. Autologous platelet rich plasma for treating chronic wounds. Cochrane Database Syst Rev. 2012;Issue 10:Art. No.: CD006899. doi:10.1002/14651858.CD006899.pub2.
4. Rayner R, Carville K, Keaton J, et al. Leg ulcers: atypical presentations and associated co-morbidities. Wound Pract Res. 2009;17(4):168–85.
5. Agale SV. Chronic leg ulcers: epidemiology, aetiopathogenesis, and management. Ulcers. 2013;Article ID 413604:
6. Shukla VK et al. Wound healing research :a perspective from India. Int J Low Extrem Wounds. 2005 Mar:4(1):7-8
7. Agale SV. Chronic leg ulcers: epidemiology, aetiopathogenesis, and management. Ulcers. 2013;Article ID 413604:9.
8. Aminian B, Shams M, Karim-Aghaee B, Soveyd M, Omrani GR. The role of the autologous platelet-derived growth factor in the management of decubitus ulcer. Arch Iranian Med. 1999;2:98–101.
9. Steed DL. Clinical evaluation of recombinant human platelet-derived growth factor for the treatment of lower extremity diabetic ulcers. Diabetic Ulcer Study Group. J Vasc Surg. 1995;21(1):71–81.
10. Driver R, Hanft J, Fylling P, et al. A prospective, randomized, controlled trial of autologous platelet rich plasma for the treatment of diabetic foot ulcers. Ostomy Wound Manage. 2006;52(6):68–87.
11. Damir A. Recent advances in management of chronic non-healing diabetic foot ulcers. JIMSA. 2011;24(4):219–23.
12. Margolis DJ et al. Healing of diabetic neuropathic fot ulcers receiving standard treatment. A meta-analysis. Diabetic care 1999:22692-5.
13. Suryanarayan S, Budamakuntla L, Khadri SIS, Sarvajnamurthy S. Efficacy of autologous platelet-rich plasma in the treatment of chronic nonhealing leg ulcers. Plast Aesthet Res. 2014;1:65-9.
14. Knighton DR, Ciresi KF, Fiegel VD, et al. Classification and treatment of chronic nonhealing wounds: Successful treatment with autologous plateletderived wound healing factors (PDWHF). Ann Surg. 1986;204:322–30.
15. Martin P. Wound healing - aiming for perfect skin regeneration. Science. 1997;276:75–81.
16. Kakudo N, Kushida S, Ogura N, Hara T, Suzuki K. The use of autologous platelet rich plasma in the treatment of intractable skin ulcer. Open J Reg Med. 2012;1:29–32.
17. Choukroum J. et al. PRF: a second generation platelet concentrate. Part4:clinical effects on tissue healing. Oral surg Oral Med Oral Patho Oral RadiolEndod. 2006Mar:101(3):e56-60.