Platelet rich fibrin dressings in the treatment of non-healing trophic ulcers of leprosy

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Accepted for publication 12 April 2018

Summary

Introduction: Trophic ulcers in leprosy are a therapeutic challenge. Various treatment options have been tried, but none is found to be universally effective. The search for better treatment continues.

Methods: Leprosy patients with long standing trophic ulcers treated with platelet rich fibrin (PRF) dressings were identified in this retrospective review. PRF was prepared by centrifuging autologous blood at 2800 rpm for 15 minutes. The PRF dressings were repeated at weekly intervals and treatment response was assessed using the National Pressure Ulcer Advisory Panel (NPUAP) staging.

Results: Ten patients (7 males) treated with PRF dressings were identified. The mean age of the study patients was 45-4 years. Three patients had NPUAP stage II, six patients had NPUAP stage III and one patient had NPUAP stage IV ulcers. Eight patients showed complete healing after 2–4 PRF dressing sessions. Complications were limited to localised infection in one patient.

Conclusion: PRF dressings are a promising therapeutic option for treatment of non-healing trophic ulcers in leprosy patients.

Keywords: Dressing, Leprosy, Platelet rich fibrin, Trophic ulcers

Introduction

Leprosy is a complex and multi-faceted disease responsible for various chronic disabilities. Foot ulceration is one of the common sequelae of the sensory-deficient foot, and its chronicity is perpetuated by repeated inadvertent trauma.1 However, little research has been published...
on its management. Treatment strategies are based on protection of the foot, in addition to varied medical and surgical measures; but nothing seems to be universally effective and the search for a better treatment options continues.

Tissue growth factors, platelet derived growth factor (PDGF) and epidermal growth factor (EGF) are reported to be useful in treating neuropathic ulcers by expediting wound healing and tissue regeneration. Platelet derived autologous products, platelets rich fibrin (PRF) and platelet rich plasma (PRP) are a rich source of these growth factors and they have been previously shown to be effective in treating non-healing, chronic leg ulcers, including neuropathic ulcers. In this study we evaluated the role of weekly PRF dressings in the treatment of non-healing, trophic leprosy ulcers.

**Material and methods**

**STUDY DESIGN**

This was a retrospective review of clinical charts of leprosy patients treated with PRF dressings for non-healing trophic ulcers from July 2015 to June 2016. The study was performed in accordance with the declaration of Helsinki and Institute Ethics Committee approval was waived for this retrospective review.

**Patients**

Leprosy patients with non-healing trophic ulcers attending the leprosy clinic of our tertiary care centre were offered treatment with PRF dressings. Non-healing was arbitrarily defined as failure to show signs of healing after 12 weeks of treatment with complete rest and sterile dressings. Patients with concurrent diabetes mellitus, hypertension, varicose veins, infection and other secondary causes contributing to the chronicity of the leg ulcer were excluded from this review. All patients were treated for leprosy and its complications with standard of care at the leprosy clinic of our institute.

**Platelet rich fibrin preparation**

PRF was prepared as per the published literature. Briefly, under aseptic precautions 5 ml of blood was collected in a sterile vial without anticoagulant. It was then immediately centrifuged at 2800 rpm for 15 minutes. At the end of centrifugation a natural fibrin matrix gel was obtained at the middle of the tube with RBC’s below and a cellular plasma at the top (Figure 1a). The fibrin gel was then placed over the ulcer base and covered with a sterile dressing to be left in-situ for 7 days (Figure 1b).

**Follow-up and treatment assessment**

All patients received weekly PRF dressings for a maximum of 5 weeks or until complete epithelization of the ulcer, whichever was earlier. At each visit, the clinical assessment was done using the National Pressure Ulcer Advisory Panel (NPUAP) staging and its modification. During the intervening period, patients were educated on foot care practices, to avoid prolonged standing, to continue taking multi-drug therapy and to use appropriate microcellular rubber footwear. Clinical images were obtained under standard conditions at each visit. Post-treatment, all patients were followed until completion of multi-drug therapy.
Results

Ten leprosy patients (four with borderline lepromatous and six with lepromatous leprosy) with trophic ulcers who were treated with PRF dressings were identified. They included seven males and three females with a mean age 45.4 years (range, 34 to 60 years) and the mean ulcer duration was 39.4 months (range: 14 to 58 months). Three patients had NPUAP stage II, six patients had NPUAP stage III and one patient had NPUAP stage IV ulcer (Figure 2a).

All ten patients had a glove and stocking pattern of anaesthesia of the extremities. The demographics and disease characteristics are summarised in Table 1.

Eight patients showed complete healing of the trophic ulcers after 2–4 PRF dressing sessions (Figure 2b). Improvement (but not complete healing) was noted in two patients at the end of five treatment sessions. Complications were limited to localised infection in one patient, who required oral antibiotics and local debridement. One patient (patient 6) with NPUAP stage IV ulcer healed up to stage 1 with five sessions of PRF. However, he relapsed after 4 months of treatment.

Discussion

Deformity and disabilities are preventable sequelae of leprosy and are strongly associated with social stigma. The recently launched WHO 5-year global leprosy strategy aims at a
reduction in the disease burden of leprosy as assessed by a decline in the number of visible deformities (Grade 2 disability, G2D) among new cases.\textsuperscript{10} One of the set targets to achieve this goal is a reduction in the rate of new G2D cases to \(<1\) case per million population. However, the current G2D rate stands at 1·7 per million population, with India accounting for 39·8\% of cases (5098 in absolute numbers).\textsuperscript{10} Trophic ulcers, one of the dreaded presentations of G2D, significantly impairs patients’ activities and is associated with considerable morbidity. The treatment strategies observed are broadly conservative and include protection of the foot and resting the affected limb for prolonged periods. However, these measures are not universally effective and there is a need for better treatment options to hasten recovery and healing.

PRP and PRF have been found useful in treating chronic ulcers of sclerodema, venous leg ulcers, diabetic foot ulcers and neuropathic ulcers.\textsuperscript{6,7} However, there is limited evidence on use of PRP and PRF in trophic leprosy ulcers. Anandan \textit{et al.} reported healing of 92\% of leprosy trophic ulcer when dressed with activated PRP at weekly intervals.\textsuperscript{11} Nagaraju \textit{et al.} reported more than 90\% improvement in seven leprosy patients treated with weekly PRF dressings for non-healing trophic ulcers. In the current study, 80\% of patients showed complete healing of trophic ulcers. Two patients showed improvement in their NPUAP ulcer stage. The improvement was apparent as early as week two and most of the ulcers re-epithelialised by 3 weeks. The healing was also supported by educational interventions on wound care practices and care of anaesthetic limbs. The relapse in one patient after five sessions of treatment was probably due to inappropriate foot-care practices following the procedure. Educational interventions on foot care practices are essential for prevention of relapses as the primary risk factor for trophic ulcer (anaesthetic limbs) persists in these patients.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure2}
\caption{(a) Pre-treatment clinical photograph (patient 6) showing NPUAP stage 3 ulcer. (b) Post-treatment clinical photograph showing complete healing after 2 sessions with PRF dressings.}
\end{figure}
Table 1. Demographics and disease characteristics of the study patient

<table>
<thead>
<tr>
<th>Patient no</th>
<th>Age</th>
<th>Sex</th>
<th>Diagnosis</th>
<th>Duration of Ulcer (months)</th>
<th>Location</th>
<th>Ulcer size, cm (baseline)</th>
<th>Ulcer size, cm (end)</th>
<th>NPUAP stage (baseline)</th>
<th>NPUAP stage (end)</th>
<th>No of sessions</th>
<th>Multidrug therapy</th>
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<td>Male</td>
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<td>0</td>
<td>3</td>
<td>On therapy</td>
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<tr>
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<td>Male</td>
<td>BL</td>
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<td>Left great toe</td>
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<td>3</td>
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</table>

BL, borderline lepromatous leprosy; LL, lepromatous leprosy.
The mechanism of wound healing with PRF/PRP is an area of intense scientific study. Platelets and platelets derived products have been explored for their various healing, regenerative and aesthetics properties in many surgical fields. The growth factors released from the α-granules of activated platelets, along with fibrin, fibronectin and vitronectin play a pivotal role in modulation of tissue repair and regeneration. These growth factors include vascular endothelial growth factor (VEGF), fibroblast growth factor-β (FGFβ), PDGF, hepatocyte growth factor (HGF), EGF, and angiopoietin-I (Ang-I) among others. The growth factors, through their autocrine and paracrine action, promote angiogenesis, tissue remodelling, recruitment of keratinocytes and mesenchymal stem cells and synthesis of the extracellular matrix.

PRF is a second-generation platelet concentrate consisting of a fibrin matrix gel polymerized in a tetra molecular structure, with incorporation of platelets, leucocytes, cytokines, and circulating stem cells. PRF has some distinct advantages over PRP. The technique of PRF preparation is simpler, involves minimal handling, does not require anticoagulant or a thrombin activator. The consumables required for PRF preparation (sterile test tubes, forceps and centrifuge machine) are easily available in a hospital setup. Further, the gel formulation of PRF is easy to apply on a raw wound compared to a liquid formulation of PRP. Studies have also shown that the concentration of growth factors is significantly higher in PRF compared to PRP and whole blood. The effects of PRP are not limited to their growth factor content alone, but many factors of healing act in complex synergy, such as leukocytes, fibrin matrix, and circulating progenitor cells. The biologic activity of the autologous growth factors along with biomechanical stiffness of plasmatic proteins after fibrin mesh formation has shown to offer a unique physiologic architecture that is very favourable to the healing process.

Our study was limited by its small sample size, retrospective study design and lack of follow-up of treated patients. Educational interventions on wound care practices and care of anaesthetic limbs would have added to the efficacy of PRF in hastening wound healing. However, our patients had previously failed these supportive measures for at least 12 weeks and the rapidity of wound healing after PRF dressings points to its definitive role. The results of our series should encourage future prospective studies to assess the efficacy of PRF dressing in trophic leprosy ulcers. Its distinctive advantages include use of autologous blood and low cost and limited resource requirement in its preparation. However, its wide spread application is still limited due to poor accessibility of health care facilities by leprosy patients, disease stigmatisation and lack of manpower resources.

References


