Platelet rich fibrin matrix the cost effective way to treat trophic ulcer in diabetes: A pilot study

Vaibhav Thorat¹, Imranali M Khan², Sakshi Gaikwad³

¹Junior Resident, Department of General Surgery, Datta Meghe Institute of Medical Sciences, Wardha, Maharashtra, India
²Associate Professor, Department of General Surgery, Datta Meghe Institute of Medical Sciences, Wardha, Maharashtra, India
³Junior Resident, Department of Dermatology, S. Nijalingappa Medical College, Bagalkot, Karnataka, India

Corresponding author
Junior Resident, Department of General Surgery,
Datta Meghe Institute of Medical Sciences, Wardha,
Maharashtra, India;
Email: vaibhavthorat93@gmail.com

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ABSTRACT

Trophic ulcers in diabetic patients are major complications leading to morbidity. These non-healing ulcers are troublesome for both patients and treating doctors and reduces quality index of life of the patients. Dressings and plastic surgical corrections of these ulcers is financial and emotional trauma to patients and requires long hospital stay. Platelet Rich Fibrin Matrix (PRFM) is easy, safe, OPD based and cost effective way to treat these ulcers. Therefore treatment of such ulcers with PRFM reduces financial burden of patients and improve quality of life.
Keywords: Platelet rich fibrin matrix (PRFM), non-healing ulcer, Diabetes mellitus, Platelet rich plasma (PRP), Platelet poor plasma (PPP)

1. INTRODUCTION
Trophic ulcer is a major complication in diabetic patients which are mainly attributed to autonomic neuropathy causing patients morbidity. Healing of such wounds is great concern due to chronic inflammation, slow healing, and senescence of reparative cells. It has various impacts on work productivity and quality of life. Often the lesions are foul smelling which causes social embarrassment. Various modes of treatments medical as well as surgical are available. Taking cost of these treatments into consideration, it causes financial burden on the people in rural area. Various conventional therapies are used for treating trophic ulcers like topical phenytoin, topical metronidazol, application of topical growth factors, saline dressing, collagen dressing, vacuum assisted closure, hyperbaric oxygen therapy, reconstructive surgeries etc along with offloading pressure from ulcer can also be a great help (Puri et al., 2012; Pitiakoudis et al., 2004; Mishra et al., 1995). There is need for simpler, cost effective treatment to lessen the duration of ulcer and the total number of dressings.

Platelet rich fibrin matrix (PRFM) is a unique, easy, cheaper, OPD based procedure. It is rich in growth factors (GF) can be used in wound healing (Steenvoorde et al., 2008; Somani and Rai, 2017). It is a matrix of fibrin with high amount of platelets, causing sustained release of various GFs, resulting in wound healing (O’Connell et al., 2006).

Objective
To demonstrate effectiveness of PRFM to treat trophic ulcer in DM

2. MATERIALS AND METHODS
The study is conducted in General Surgery department at a tertiary care center in central India. Ethical committee permission was taken prior to the study and written informed consent was obtained from all the study participants. The study was done from March 2019 to November 2019. Total of 50 patients were included in our study. Age of the patients ranged from 15years to 75 years. 35 were male and 15 were females.

All consecutive trophic ulcers patients suffering from diagnosed trophic ulcer due to diabetes were included. Patients with age below 15 years, having history of anemia, bleeding disorders, other hematological disorders, patients on anticoagulants, uncontrolled diabetes, pregnant, lactating mother and with malignant ulcers, patients suffering from HIV, HbsAg positive were excluded from the study.

Procedure
Pre-treatment photographs were taken (Figure 1). Ulcer with prior infection was taken care with antibiotics. Ulcer size in the form of length, breath was measured and area was calculated.

![Figure 1 Pretreatment photograph](image-url)
Under strict aseptic precaution 10ml of venous blood was transferred to sterile centrifugation tube without the anticoagulants. This tube was subjected to centrifugation at 3000 rpm for ten minutes. There after 3 layers were obtained: The upper most straw colored platelet poor plasma (PPP), The Red colored lower fraction with red blood cells (RBCs) and the middle fraction is containing the PRFM (figure 2-9).

Figure 2 Three layers obtained after centrifugation

Figure 3 Separated PRFM from upper layer (straw colored) on a gauze piece

Figure 4 Separated PRFM from upper layer and lower layer with retained erthrocyte layer about 1mm on a gauze piece.

The upper straw colored layer was discarded, with the help of scissors and forceps PRFM layer was separated from RBC layer, preserving a small layer of RBC layer (1mm). This was then transferred to sterile gauze. This gauze is then transferred or gently applied on the ulcer followed by non-absorbable dressing. Secondary dressing and dried PRFM was removed after five days. Every weekly the procedure is repeated for five weeks. Area was calculated and serial photographs were taken at each visit. Area was calculated by using formula for ellipse: length x breath x0.7854 because ellipse is closer to wound shape (Blume et al, 2008).
Figure 5 Ulcer after 1\textsuperscript{st} sitting

Figure 6 Ulcer after 2\textsuperscript{nd} sitting

Figure 7 Ulcer after 3\textsuperscript{rd} sitting

Figure 8 Ulcer after 4\textsuperscript{th} sitting
3. RESULTS

A total of 50 ulcers were treated with PRFM. Out of which 35 (70%) were male and 15 (30%) were females (table 1).

**Table 1** Distribution of patients depending on gender

<table>
<thead>
<tr>
<th>Gender</th>
<th>Number of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>35</td>
<td>70%</td>
</tr>
<tr>
<td>Female</td>
<td>15</td>
<td>30%</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>100%</td>
</tr>
</tbody>
</table>

Mean age of the patients in our study was 52.36 years.

**Table 2** Distribution of patients depending on age

<table>
<thead>
<tr>
<th>Age</th>
<th>Number of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>15 to 35 years</td>
<td>2</td>
<td>4%</td>
</tr>
<tr>
<td>36 to 55 years</td>
<td>36</td>
<td>72%</td>
</tr>
<tr>
<td>56 to 75 years</td>
<td>12</td>
<td>24%</td>
</tr>
</tbody>
</table>

Baseline area was calculated for each patient by using formula for ellipse: length x breath x0.7854 because ellipse is closer to wound shape (Blume et al., 2008) (table 2).
Table 3 Distribution of patients depending on baseline area of ulcer

<table>
<thead>
<tr>
<th>Baseline area of ulcer</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 to 5 sq.cm.</td>
<td>7</td>
</tr>
<tr>
<td>5 to 10 sq.cm.</td>
<td>32</td>
</tr>
<tr>
<td>10 to 15 sq.cm.</td>
<td>7</td>
</tr>
<tr>
<td>15 to 20 sq.cm.</td>
<td>4</td>
</tr>
</tbody>
</table>

Baseline area of ulcer calculated after each sitting of PRFM. Total 28 patients showed 100% improvement 1 week after the second sitting. Total 10 patients showed 100% improvement 1 week after third sitting. Total 4 patients showed 100% improvement 1 week after forth sitting. Total 2 patients showed 100% improvement 1 week after fifth sitting (table 3 & graph 1).

Table 4 Distribution of patients depending on sitting required for complete healing of ulcer

<table>
<thead>
<tr>
<th>Complete healing of ulcer</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>After 1st sitting</td>
<td>0</td>
</tr>
<tr>
<td>After 2nd sitting</td>
<td>28</td>
</tr>
<tr>
<td>After 3rd sitting</td>
<td>10</td>
</tr>
<tr>
<td>After 4th sitting</td>
<td>4</td>
</tr>
<tr>
<td>After 5th sitting</td>
<td>2</td>
</tr>
</tbody>
</table>

Graph 2 Distribution of patients depending on sitting required for complete healing of ulcer

Total 4 patients didn’t show 100% improvement after fifth sitting. Healing showed by those four patients are 90%, 86%, 82% and 70% respectively. Two patients from our study lost to follow-up after 1st sitting. The mean percentage improvement in the area after 5 sittings is 94.56%. All the ulcers were closed by maximum of fifth sitting. No adverse event was reported as a result of PRFM. The volume of blood withdrawn (10ml) was sufficient for all the ulcers (table 4 & graph 2).

4. DISCUSSION

Trophic ulcer is most common complication of diabetes affecting the quality of life of the patients. By assisting in healing process of such ulcers can improve the quality of life. PRFM has the potential and is inexpensive means for treating such ulcers (Steenvoorde et al., 2008). It releases growth factors for 1 week in a slow and controlled way once applied on the ulcer area. The mean concentration of growth factors in PRFM was three times that of PRP (Yazawa et al., 2003; Dohan et al., 2006). PRFM is a second generation of platelet concentrate. It is a simple, cost effective process with no complex handling and there is no use of anticoagulant as used in platelet rich plasma (Naik et al., 2013). PRFM is rich in platelets and cytokines. These platelet release various growth factors like...
platelet derived growth factors, transforming growth factor- beta, basic fibroblast growth factors, insulin like growth factors, platelet derived endothelial growth factors etc. These growth factors play a crucial role in repair and regeneration or act as a stimulus for the process of healing (O’Connell et al., 2006).

In our study, we found very significant improvement in the size and area of the ulcer from the second week itself. Out of 50 patients, 28 showed 100% improvement within one week after the second sitting. Total 10 patients showed 100% improvement 1 week after third sitting. Total 4 patients showed 100% improvement 1 week after forth sitting. Total 2 patients showed 100% improvement 1 week after fifth sitting. Total 4 patients didn’t show 100% improvement after fifth sitting. Improvement of the ulcer was assessed by taking photograph and measuring area (ellipse: length x breath x 0.7854) before every sitting. According to Nagaraju et al. mean percentage of improvement in the area of ulcer was 93.52%. All ulcers closed by a maximum of five sittings. PRFM for the treatment of trophic ulcers in treated patients with Diabetes mellitus is a feasible, safe, simple and inexpensive method (Nagaraju et al., 2017). Steenvoorde et al. achieved full closure in eight wounds and a reduction in diameter of ulcer by up to 66% in three wounds, while the remaining two wounds only showed a reduction in depth with a mean number of 2.2 applications (Steenvoorde et al., 2008). In a study by Goda, the rate of complete closure in PRF group with initial size of more than 10 sq.cm was 50% at the sixth week and 100% at the seventh week (Goda, 2018). Somani and Rai reported that the complete closure of the ulcers in the PRF group (Somani and Rai, 2017). As compared to above mention studies our study showed complete healing with 100% improvement, the reason can be due to the size of the ulcers or the study carried out on smaller number of patients.

Limitation of the study was the short duration of treatment restricted to 5 weeks. Ulcers with comparatively larger size, and more number of patients might have given more information regarding the effectiveness of PRFM in healing trophic ulcer.

5. CONCLUSION

PRFM is an easy, safe, cost effective and feasible procedure. It is OPD procedure, in which blood is withdrawn from the patient itself without adding any anticoagulant. It was found to enhance the healing process of the ulcers without any side effects. As ours it was pilot study, more randomized control studies are required to appreciate the effects of PRFM.

Funding

This research received no external funding.

Conflicts of Interest

The authors declare no conflict of interest.

Informed consent

Written and oral informed consent was obtained from all individual participants included in the study. Additional informed consent was obtained from all individuals participants for whom identifying information is included in this manuscript.

Ethical approval for study

The study was approved by Medical Ethics Committee of Datta Meghe Institute of Medical Sciences (DU). Ethical approval code is DMIMS (DU)/IEC/2018-19/7411.

REFERENCE