Management of diabetic foot ulcers with platelet rich plasma: A clinical study

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Abstract

Background: Diabetic foot is a frequent site for complication in DM. Ulceration occurs as a result of trauma in the presence of neuropathy and/or peripheral vascular disease with infection as a secondary phenomenon following disruption of the protective epidermis. The study was conducted to determine the role of autologous platelet rich plasma in healing of diabetic foot ulcers.

Materials & Methods: The present study was conducted on 20 cases of diabetic foot ulcers. In all patients, ulcer size as per maximum length and breadth and area were recorded and two PRP dressings were given on day 0 and second after first week. The size was measured in maximum length and maximum breadth by using a scale and area was calculated.

Results: Out of 20 patients, males were 10 and females were 10. The difference was non-significant (P-1). Age group 30-50 years had 2 males and 1 females, 50-70 years had 3 males and 5 females and >70 years had 5 males and 4 females. The difference was significant (P-0.05). There was <60% reduction in 1 male, 61-70% reduction in 1 male and 1 female, 71-80% reduction in 2 males and 4 females and >80% reduction in 6 males and 5 females. The difference was significant (P<0.05).

Conclusion: PRP seem to be an effective and safe preparation used for therapy of DFU. PRP is an autologous product, therefore constitutes no risk of viral hepatitis or HIV infection.

Keywords: Diabetic foot, platelet rich plasma, wound

Introduction

Diabetes mellitus is a metabolic disorder characterized with increased blood glucose level. It may be due to decrease insulin level in the body or due to inability of insulin receptors to act. Patient with diabetes is vulnerable to various complications. There are several complications of DM. Among all, diabetic foot ulcer, diabetic neuropathy, diabetic nephropathy, diabetic retinopathy and diabetic foot ulcer are common [1].

Diabetic foot is a frequent site for complication in DM. Ulceration occurs as a result of trauma in the presence of neuropathy and/or peripheral vascular disease with infection as a secondary phenomenon following disruption of the protective epidermis. The disease often leads to the development of serious health threatening complications. Of all diabetic complications, diabetic foot syndrome (DFS) is one of the most devastating [2].

In 15-25% of DM patients, diabetic foot ulceration (DFU) develops. Approximately 10-25% of those cases require amputation. Studies have shown that amputation is 20-35 times higher among patients with diabetes than without it. It has been observed that more than 65% of diabetic foot ulcers are the result of underlying neuropathy. One of the more commonly described mechanisms of action is the polyol pathway. Peripheral arterial disease (PAD) is a contributing factor to the development of foot ulcers in up to 50% of cases [3].

Among various treatment modalities for diabetic foot ulcers, use of autologous platelet-rich plasma (PRP) in the form of local application obtained by centrifugation of whole blood and addition of an activator, clotting agent is designed for the creation of local conditions favourable to healing processes [4]. The present study was conducted to determine the role of autologous platelet rich plasma in healing of diabetic foot ulcers.

Materials & Methods

The present study was conducted in the department of orthopedics. It comprised of 20 cases of both genders. All were informed regarding the study and written consent was obtained.
Ethical clearance was obtained from institutional ethical committee prior to the study. Patient with liver cell failure, patient with severe cardiomyopathy and patient with major lower limb amputation were excluded from the study. General information such as name, age, gender etc. was recorded. In all patients, ulcer size as per maximum length and breadth and area were recorded and two PRP dressings were given on day 0 and second after first week. The size was measured in maximum length and maximum breadth by using a scale and area was calculated. Assessment of the DFUs was done as per University of Texas classification of DFU. Results thus obtained were subjected to statistical analysis for correct inferences. P value less than 0.05 was considered significant.

**Results**

**Table 1: Distribution of patients**

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Males</th>
<th>Females</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total- 20</td>
<td>10</td>
<td>10</td>
<td>1</td>
</tr>
</tbody>
</table>

Table 1 shows that out of 20 patients, males were 10 and females were 10. The difference was non-significant (P=1).

**Table 2: Age wise distribution of patients**

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Males</th>
<th>Females</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-50</td>
<td>2</td>
<td>1</td>
<td>0.05</td>
</tr>
<tr>
<td>50-70</td>
<td>3</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>&gt;70</td>
<td>5</td>
<td>4</td>
<td></td>
</tr>
</tbody>
</table>

**Graph 1: Reduction in length and breadth of ulcer in patients**

Graph 1 shows that there was <60% reduction in 1 male, 61-70% reduction in 1 male and 1 female, 71-80% reduction in 2 males and 4 females and >80% reduction in 6 males and 5 females. The difference was significant (P<0.05).

**Discussion**

Diabetes mellitus is a disorder characterized by presence of multiple complications such as diabetic neuropathy, nephropathy, retinopathy and peripheral vascular disease etc. Uncontrolled diabetes contributes to the development of neuropathy and peripheral arterial disease by complex metabolic pathways. Loss of sensation caused by peripheral neuropathy, ischaemia due to peripheral arterial disease, or a combination of these may lead to foot ulcers. Leg ulcers are classified as acute or chronic according to the duration. Chronic ulcers come with significant cost and morbidity for the patients and society. These non-healing ulcers of lower extremity develop as a result of peripheral neuropathy, ischemia, or trauma and are often difficult to treat \([5]\).

In present study, out of 20 patients, 10 patients were seen each in males and females. We found that age group 30-50 years had 2 males and 1 females, 50-70 years had 3 males and 5 females and >70 years had 5 males and 4 females. This is in agreement with Junichi et al. \([6]\).

Vickie et al. \([7]\) in their study, 24 patients with non-healing ulcers of different etiologies were treated with single dose of subcutaneous PRP injections along with topical application of PRP gel under compassionate use. The mean age was 62.5±13.53 years and 24 weeks follow up period was used in the study. All the patients showed signs of wound healing with reduction in wound size, and the mean time duration to ulcer healing was 8.2 weeks. There was 5 fold increases in the platelet concentrate in the final PRP product obtained using the rapid point-of-care device, and the average platelet dose administered to the patients was 70.10×10^11.

PRP contains additionally leukocytes that increase its antibacterial properties and synthesize interleukins as part of a nonspecific immune response. Platelets contain numerous natural growth factors released from their a granulations and stimulating healing processes. PDGF is a growth factor found also in macrophages and endothelial cells. TGF is also found in macrophages, monocytes, and keratinocytes. VEGF is found mostly in endothelium, and IGF-1 is predominantly produced in the liver \([8]\).

In present study, there was <60% reduction in 1 male, 61-70% reduction in 1 male and 1 female, 71-80% reduction in 2 males and 4 females and >80% reduction in 6 males and 5 females. This is in agreement with Knighton et al. \([9]\).

It has been observed that the antibacterial effect of PRP is a result of activity of PGDF, by activation of macrophages, and VEGF, by stimulation of macrophages and monocytes. Re-epithelialisation and fibroblast proliferation are mostly the effect of PDGF, TGF, EGF, and IGF-1, stimulating the deposition of extracellular matrix (ECM). PDGF and IGF-1 are responsible for stimulation of other growth factors and cytokines, and angiogenic effect is shown mostly by VEGF, EGF, and PDGF \([10]\).

Sunil et al. \([11]\) conducted a study on 50 patients of chronic non-healing ulcers who were grouped into two groups-PRP and conventional dressing group of 25 patients each. PRP group showed better results in term of healing rate and required significantly less number of dressings for wound closure. Authors suggested that PRP is a safe and effective treatment modality for chronic non-healing ulcers. PRPT is a rich source of locally active growth factors and cytokines that improve conditions of wound healing. Relatively simple and cheap production of PRP argues for continued interest in that adjunct method. It seems that specific cellular therapy constitutes an additional and valuable option in therapy of DFU resistant to the conventional therapy.

**Conclusion**

PRP seem to be an effective and safe preparation used for therapy of DFU. PRP is an autologous product, therefore constitutes no risk of viral hepatitis or HIV infection.
References


