Transfusion and Apheresis Science 56 (2017) 160–164

Contents lists available at ScienceDirect

Transfusion and Apheresis Science

journal homepage: www.elsevier.com/locate/transci

Evaluation of wound healing in diabetic foot ulcer using platelet-rich plasma gel: A single-arm clinical trial

Mohammad Hossein Mohammadi[a], Behnam Molavi[b], Saeed Mohammadi[c,*], Mohsen Nikbakht[c], Ashraf Malek Mohammadi[c], Shayan Mostafaei[c], Amir Hossein Norooznezhad[c], Ali Ghorbani Abdegah[b], Ardeshir Ghavamzadeh[c]

[a] BMT and Cell Therapy Center of Taleghani Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[b] Surgery Department, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran
[c] Hematology, Oncology and Stem Cell Transplantation Research Center, Tehran University of Medical Sciences, Tehran, Iran

ARTICLE INFO

Article history:
Received 24 August 2016
Received in revised form
29 September 2016
Accepted 28 October 2016

Keywords:
Diabetes
Diabetic foot ulcer
Platelet-rich plasma
Wound healing

ABSTRACT

The aim of the present study was to evaluate the effectiveness of using autologous platelet-rich plasma (PRP) gel for treatment of diabetic foot ulcer (DFU) during the first 4 weeks of the treatment. In this longitudinal and single-arm trial, 100 patients were randomly selected after meeting certain inclusion and exclusion criteria; of these 100 patients, 70 (70%) were enrolled in the trial. After the primary care actions such as wound debridement, the area of each wound was calculated and recorded. The PRP therapy (2 mL/cm^2 of ulcers) was performed weekly until the healing time for each patient. We used one sample T-test for healing wounds and Bootstrap resampling approach for reporting confidence interval with 1000 Bootstrap samples. The p-value < 0.05 were considered statistically significant. The mean (SD) of DFU duration was 19.71 weeks (4.94) for units sampling. The ratio of subjects who withdrew from the study was calculated to be 2 (2.8%). Average area of 71 ulcers in the mentioned number of cases was calculated to be 6.11 cm^2 (SD: 4.37). Also, the mean, median (SD) of healing time was 8.7, 8 weeks (SD: 3.93) except for 2 mentioned cases. According to one sample T-test, wound area (cm^2), on average, significantly decreased to 51.9% (CI: 46.7–57.1) through the first four weeks of therapy. Furthermore, significant correlation (0.22) was not found between area of ulcers and healing duration (p-value > 0.5). According to the results, PRP could be considered as a candidate treatment for non-healing DFUs as it may prevent future complications such as amputation or death in this pathological phenomenon.

1. Introduction

Diabetic foot ulcer (DFU) is a common accompanying complication and the most important cause of hospitalization among diabetic patients. This phenomena, with an incidence of 15% in diabetic population, is an important issue for health and care services [1–3]. During the lifetime of a diabetic patient, the risk of any lower extremity involvement with DFU is estimated to be about 25%, which is affected by several risk factors including arterial disorders, peripheral neuropathy and infection. Among diabetic patients, 20% are diagnosed with inadequate blood flow and 50% with peripheral neuropathy. These incidences are highly significant in DFU population because 80% of them are suffering from both conditions [4]. Moreover, the vascular problems in these cases not only postpone the wound healing process but also hinder the reaction of the immune system to the accompanying infections. The vascular complications in diabetic patients mostly develop as 3 major disorders of thrombosis or arteritis of arterioles, peripheral neuropathy (mostly due to the ischemic situations) and atherosclerosis of arteries. Besides the mentioned risk factors, physical and mechanical traumas causing neuropathy in lower extremity may also lead to DFUs [5–7]. Chronic DFU is defined as an ulcer not decreased by 50% of the primary size during a month [4]. Proper treatments suggested for DFU mostly include local actions such as ulcer debridement, antibiotic therapy and bedside surgery [8,9]. Although ulcer debridement is suggested as the primary step, it could only be helpful when the patient does not suffer from arterial insufficiency. So far, different surgical methods such as percutaneous transluminal angioplasty [10], luminal stenting and arterial reconstruction surgery have been practiced in order

* Corresponding author. Hematology, Oncology and Stem Cell Transplantation Research Center, Tehran University of Medical Sciences, Tehran, Iran. Fax: +982188004140.
E-mail address: saeedm_58@yahoo.com (S. Mohammadi).

http://dx.doi.org/10.1016/j.transci.2016.10.020
1473-0502/

to improve blood supply in patients with ischemic DFUs [11,12]. Moreover, new strategies such as hyperbaric oxygen therapy [13], bioengineered tissues [14], electrical stimulation, phototherapy [15] and platelet derived growth factors [16] are also recommended and applied. Platelet derived growth factors, which have been available clinically since 1985, are biologic active compounds acting in different mechanisms and pathways including activation or induction of chemotaxis, cellular proliferation and angiogenesis to induce and accelerate wound healing [17].

The aim of this longitudinal and single-arm clinical trial was to evaluate the effectiveness of using autologous PRP gel for treatment of DFU during the first 4 weeks of treatment.

2. Materials and methods

2.1. Ethics

This clinical trial was approved by the Medical Ethics Committee of Research Institute for Hematology, Oncology and Stem Cell Transplantation of Shariati Hospital, Tehran University of Medical Sciences (approval code: 1394.103.3). Also all the team members considered the 1975 Declaration of Helsinki and its following revisions during the trial. The aim of this study was clearly explained to each patient. After the purpose of the study was explained (according to the patients' level of understanding), eventually, all patients were requested to sign a written consent form to declare that they were joining this study freely. This clinical trial was registered in the Iranian Registry of Clinical Trials (under supervision of the Ministry of Health and Medical Education) with IRCT2015123018842N10 number. Current study originally was a part of a bigger trial which unfortunately was canceled and removed from IRCT due to financial problems. Thus we had to submit for another IRCT code. During the study, however, this trial was under the supervision of the Ethics Committee.

2.2. Study design and patients

This longitudinal and single-arm clinical trial was conducted between May 2014 and December 2015 in Shariati Hospital (Tehran University of Medical Sciences, Tehran, Iran). In the mentioned period of time, 100 patients with chronic DFUs were selected in the study by simple random sampling. Then the inclusion and exclusion criteria were applied to all patients. Chronic DFU, as defined before, is a wound found in the lower extremity (usually a foot) of a known diabetic patient, which has not decreased by 50% of the primary size in one month (inclusion criteria). No other limitations such as age, sex, fasting blood sugar (FBS) or hemoglobin A1C (Hb A1C) levels were applied. Exclusion criteria included osteomyelitis, malignant arterial insufficiency, exposed bone in an ulcer, antibiotic resistance DFU, wounds with Charcot deformity, history of anti-proliferative medication or radiation in past 3 months, serum Hb < 10 mg/dL, platelet count < $10^3/\mu L$ and history of growth factor therapy within last 2 weeks. Finally, according to exclusion criteria, 70 (70%) patients as units sampling were enrolled in the trial (Fig. 1).

2.3. Primary care

First of all, demographic data and full medical history including the present illness and drug history were collected from all patients. Then primary laboratory tests such as FBS and HbA1C were re-checked. For those patients with imbalanced glucose level (abnormal FBS and/or Hb A1C), new insulin prescriptions were ordered by consulting with an expert endocrinologist while consequent laboratory results were evaluated again. For the infection complications, a specialist was consulted with to prescribe proper

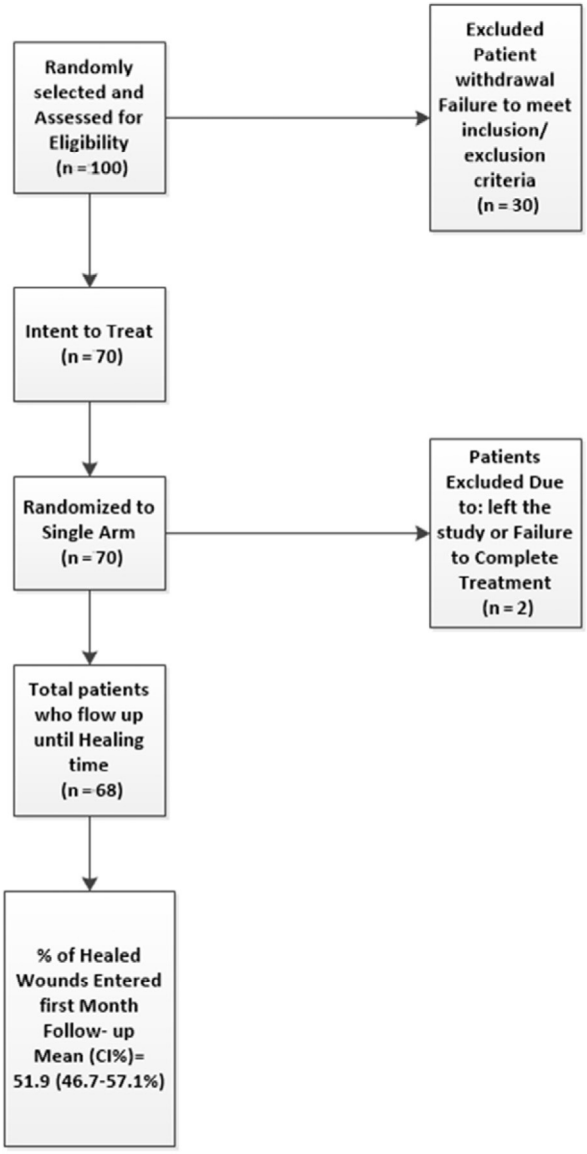

Fig. 1. A follow-up diagram of study design and methodology.

antibiotics for prophylaxis in all cases (intravenous or oral). Also debridement was performed wherever required by an expert surgeon under sedation (in some cases) in an operating room in order to remove all necrotic tissues, foreign bodies and sinuses. Afterward, the area (length and wide) of the ulcer was measured and recorded separately for each patient by a trained physician in order to find the ulcer area. For each ulcer, the most likely geometric shape was estimated and then the area was calculated according to the appropriate shape formula (such as triangle, square, rectangular or elliptic).

2.4. Platelet rich plasma preparation

PRP preparation was performed by Rooyagen PRP Gel kit (Arya Mabna Tashkhis Co, Iran). According to kit instructions, first, 27 mL of peripheral blood was drawn from donor using a 30 mL syringe containing 3 mL anticoagulant: sodium citrate. Then, the blood was shaken gently 4 times. Afterward, it was transferred into three 10 mL tubes using the transfusion kit adaptor connected to the syringe, and centrifuged in 2000 × *g* for 10 minutes in 24 °C. After first centrifugation, the 2 fold rich platelet in the supernatant