Transfusion and Apheresis Science 56 (2017) 226–232

Contents lists available at ScienceDirect

Transfusion and Apheresis Science

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

International Forum

Evaluation of platelet-rich plasma gel potential in acceleration of wound healing duration in patients underwent pilonidal sinus surgery: A randomized controlled parallel clinical trial

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ARTICLE INFO

Article history:
Received 1 November 2016
Received in revised form
25 December 2016
Accepted 27 December 2016

Keywords:
Platelet-rich plasma
Pilonidal sinus
Wound healing
Angiogenesis

ABSTRACT

Objectives: One of the most important surgical issues applied in the treatment of pilonidal sinus disease is wound healing. The aim of this study was to investigate the possible effect of platelet-rich plasma (PRP) gel on accelerating wound healing in these patients.
Methods: In this randomized, controlled, parallel group clinical trial, 110 patients were randomly allocated into two parallel groups with the same size (controls and treatment arm) after meeting inclusion and exclusion criteria. After the surgery, controls were treated by classic wound dressing while the case group was treated with PRP gel in a classic wound dressing platform. The patients were then evaluated for duration of antibiotics consumption, experienced pain and the time of returning to routine activities. Also, both groups were assessed for angiogenesis (by detecting $CD34^+$ cells using immunohistochemical assay) and collagen sedimentation (masson's trichrome staining) using pre-complete healing wound biopsy. All the statistical analyses were performed using SPPS 20 and p-values of less than 0.05 considered statically significant.
Results: According to the results, patients treated with PRP gel went through a significantly faster healing process (8.69 ± 1.18 in controls and 4.78 ± 0.87 weeks in PRP gel treated ones with the P-value = 0.03) and returned to their routine activities (3.3 ± 0.64 for the treatment of arm and 6.5 ± 1.03 weeks for controls with the P-value = 0.00) while experiencing less pain (P-value = 0.00) and shorter anti-biotic consumption duration (P-value = 0.00).
Conclusion: Considering the results, authors of this study suggest PRP gel treatment for post operation wound dressing of pilonidal sinus disease with healing by secondary intention.

1. Introduction

Pilonidal disease is a sinus or an abscess diagnosed in the midline of natal cleft in the sacrococcygeal area with a distance of 5–8 cm away from anus [1]. Pilonidal disease with the incidence of 26 per 10,0000 individuals is twice as common in males [2] and mostly occurs after puberty with the peak of 19 and 22 years in females and males, respectively. On the other hand, visiting a patient with pilonidal disease after 40 years is rare [3]. This disease comes with comorbid disorders associated with pain and discomfort in these patients, usually leading to interruption of both personal and social life of the patients [4,5]. So far, several risk factors such as obesity, local trauma, white race, positive family history, high amount of body hair and sedentary jobs are showed to interfere with the occurrence of this disorder [6]. The first line treatment for complex and recurring cases is surgery performed in different methods such

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http://dx.doi.org/10.1016/j.transci.2016.12.032
1473-0502/

as incision and drainage, excision with primary closure and excision with flap reconstruction [7]. According to numerous studies, patients under open healing secondary intention situation experienced lower rate of recurrence but longer healing process period in comparison to other methods such as primary surgical closure [2]. Regarding the secondary intention method, since the excision is of a wide field of surface and the surface will be left open, the most important post operation issue is how to accelerate wound healing [8–11]. Therefore, the search for a treatment with minimal pain, accelerated healing time and a short span of time for returning to the normal daily activities is vastly pursued [2].

Platelet-rich plasma (PRP), as it implies, is a very rich in platelet derived autologous product [12]. Platelet related products have been used in wound healing since 1985 [13] with a so far satisfactory outcome in the treatment of chronic skin and soft tissue lesions [14], maxillofacial [15] and plastic surgeries [16,17] by presenting high amounts of growth factors and chemokines [14].

Along with these lines, the aim of this study was to investigate the potential of PRP gel therapy in accelerating wound healing of those patients who underwent surgery for pilonidal sinus disease.

2. Materials and methods

2.1. Ethical standards

Both hospital and University Medical Ethic Committees approved the study. Also all of the team members have abided 1975 Declaration of Helsinki and its next revisions. Before enrolling any patient in the study, all of them signed a written consent form freely after being explained the aim, methods, benefits and any possible risk of this study as well as other issues according to their knowledge. This study was approved by Iranian Registry of Clinical Trials (under supervision of Ministry of Health and Medical Education) with the license number of IRCT2016020418842N11.

2.2. Study design and participants

This randomized, controlled, parallel group clinical trial was conducted between June 2012 and September 2015 in a teaching hospital (the corresponding authors' affiliation). Patients diagnosed with pilonidal sinus disease with a scheduled surgery (including criteria) were enrolled in this study. They were then allocated into the control and PRP treatment parallel groups by random selection using randomly permuted blocks method (block size was two, but the investigators were blind). Also, for those patients in PRP group an exclusion criteria was defined as follows: lower platelet count of $<10^3/\mu L$, hemoglobin <10 mg/dL, anti-proliferative therapies such as chemotherapy in the past 3 months, anti-inflammation medications in the past 2 weeks, radiation in the past 3 months, growth factor therapies in the last 2 weeks, history of diabetes, history of mal-absorption (celiac disease) and any contra-indication in peripheral venues access. A follow diagram of study design is shown in Fig. 1.

2.3. Surgery

First, the process of surgery was explained to all patients. Patients with previous heart disease history, mentionable positive history of smoking and any clinical suspicion were referred to cardiovascular and anesthesiologist experts for pre-operative evaluations. They received a single dose of Cefazolin as prophylaxis and placed in prone position, then prep and drape were performed. The sinus was resected with an elliptical incision containing the sinus orifice until the presacral fascia borderline was achieved under general anesthesia. Then the homeostasis performed after mentioned actions. All the operations were performed by an expert surgeon with 10 years of experience (Figs. 2–4).

After the surgery, the wound was filled using normal saline solution and then redrainage in order to find the wound volume. This step was performed in order to estimate the proper amount of PRP for injection as well as measuring wound volume for further evaluations.

2.4. Platelet rich plasma gel preparation

PRP preparation was performed by Rooyagen™ PRP-Gel kit (Arya Mabna Tashkhis Co, Iran). According to Kit instructions, first, 27 mL 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. Afterwards, it was transferred into three 10 mL tubes using the transfusion Kit adaptor connected to the syringe, and centrifuged in $2000 \times g$ for 10 min in 24 °C. After first centrifuge, the 2 fold rich platelet in the supernatant plasma was achieved. This PRP was then transferred to second tube containing 2 mL 25 mM CaCl2 leading to gel formation after 20 min. Finally, the platelet gel was applied topically on the wound which would be explained in details in the next step. In order to prepare other amounts of PRP it was tried to follow a similar ratio according to the above instructions. Average count of platelets in PRP was 10^7/mL.

2.5. Wound dressing and evaluation

The control group only underwent the classic dressing with absorbent sterile cotton gauze. For the treatment group, PRP was injected to a 13 mm-depth of the wound area (0.1 cc/cm^2) while for controls normal saline were injected. The injection was preformed right after surgery and continued weekly. After each injection, the wound was filled with PRP mixed with 0.9% $CaCl_2$ in a ratio of 4/1 to make a gel PRP gel. Then, the surface was covered using sterile non-allergenic latex in order to inhibit any gel leakage for 24 h. After 24 h, the latex cover was removed and the usual dressing was performed. This method for the treatment arm was performed until the healing was achieved. For both groups, wound washing with normal saline (0.9%) was ordered twice a day. Wound debridement was also done in order to remove the necrotic tissues whenever necessary.

2.6. Pain and antibiotic evaluations

As mentioned, before surgery a single dose of cefazolin was administrated for all patients. After that for 3 days cefalexin was prescribed as a post operative prophylaxis. In case of infection which is not rare in patients with primary intention ciprofloxacin and clindamycin were prescribed until the proper clinical results. The consumption of antibiotic by patients was extracted from their clinic files following an interval of 3 days, 6 days, 1 week and 2 weeks. Moreover, the duration of pain in both groups was recorded according to patient's declaration. Also all patients were asked to express when they are able to go back to routine life in week(s).

2.7. Wound biopsy

According to the signed consent forms taken from the patients, a wound biopsy must have been done few days before the complete healing was achieved in order to evaluate the histological differences between two groups. An incisional biopsy was done under the sterile situation. The tissue was evaluated for neovascularization using immunohistochemistry (IHC) assay of $CD34^+$ (BD Pharmingen™, purified rat anti-CD34) positive cells in order to