

The efficacy of autologous platelet-rich plasma combined with erbium fractional laser therapy for facial acne scars or acne

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Received November 27, 2012; Accepted February 20, 2013

DOI: 10.3892/mmr.2013.1455

Abstract. The aim of this study was to evaluate the efficacy of autologous platelet-rich plasma (PRP) combined with erbium fractional laser therapy for facial acne or acne scars. PRP combined with erbium fractional laser therapy was used for the treatment of 22 patients, including 16 patients who suffered from facial acne scars and 6 patients who suffered from acne scars concomitant with acne. Whole blood (40 ml) was collected from each patient, and following differential centrifugation, PRP was harvested. After using an erbium fractional laser, we applied PRP to the entire face of every patient. Digital photos were taken before and after the treatment for evaluation by dermatologists and the patients rated the efficacy on a 5-point scale. The erythema was moderate or mild, while its total duration was <3 days; after receiving the treatment three times, 90.9% of the patients showed an improvement of >50%, and 91% of the patients were satisfied; no acne inflammation was observed after treatment. PRP combined with erbium fractional laser therapy is an effective and safe approach for treating acne scars or acne, with minimal side-effects, and it simultaneously enhanced the recovery of laser-damaged skin.

Introduction

Acne occurs in all areas of the body with high concentrations of pilosebaceous glands, but occurs on the face, back and chest in particular. Inflammatory acne lesions may result in permanent scars, the severity of which may depend on delays in treating acne patients. The prevalence and severity of acne scarring in the population has not been well studied, although the available literature usually shows that it is correlated with the severity of acne (1). A study of 2,133 volunteers aged 18-70 from the general population showed that almost 1% of people had acne scars, although only 1 in 7 of these individuals were considered to have 'disfiguring scars' (1). Severe scarring caused by acne is associated with substantial physical and psychological distress, particularly in adolescents. There are many treatments for acne or acne scars, particularly fractional laser therapy. Fractional laser therapy has been shown to be an effective treatment method for acne or acne scars; however, it is associated with a long period of erythema and edema (5-10 days), which may hinder patients' daily lives.

Autologous platelet-rich plasma (PRP) is the plasma portion of autologously sourced blood with an iatrogenically high platelet concentration, which is extensively used to promote soft and hard tissue healing and to significantly reduce wound-healing time (2-4). At sites of tissue damage, platelets are the first cells to arrive and play an important role in mediating tissue repair through the release of growth factors (GFs), such as PDGF, TGF- β , EGF, VEGF, IGF and FGF, from their α -granules (5,6). These factors are known to regulate cell migration, attachment, proliferation and differentiation, and to promote extracellular matrix accumulation via binding to specific cell surface receptors (7). Adding autologous thrombin and calcium ions triggers the activation process. Once platelets are activated, secretion of GFs begins within 10 min and 95% of all factors are secreted within 1 h (8). Furthermore, PRP is easily obtained from autogenous whole blood by two centrifuging steps. At present, PRP is extensively used for bone cartilage tissue regeneration, soft tissue healing wound healing, and cosmetic and maxillo-facial surgery, and the effects in the clinic are positive (2,9,10).

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Key words: fractional laser, platelet-rich plasma, acne, scar

The 2,940-nm erbium fractional laser has photothermal and mechanical effects (11). It removes the abnormal tissue and rough epidermal through tissue vaporization. It induces collagen regeneration and remodeling in the dermal layer while epidermal stem cells located in the hair follicle and surrounding residual skin island proliferate, until the wound is healed (12). The objective of our study was to evaluate whether the combination of autologous PRP and 2,940-nm erbium fractional laser therapy increases the treatment effect for facial acne or acne scars and reduces the adverse effects.

Materials and methods

Participants. In total, 22 participants with moderate to severe facial acne or acne scars (including 16 patients who suffered from facial acne scars and 6 patients who suffered from acne scars with concomitant acne) were enrolled in this study. The mean participant age was 28 (range, 19-39 years), and the sample included 17 females and 5 males. The study reported on the skin type of the subjects using the Fitzpatrick skin type classification and subjects had either skin type III or IV. Participants were excluded if they reported a history of keloid scar formation, any active inflammation, oral isotretinoin use within the preceding 6 months, diabetes, collagen vascular disease, or ablative or nonablative laser skin resurfacing within the preceding 12 months, or if they were pregnant or lactating.

This study was conducted in accordance with the Declaration of Helsinki and with approval from the Ethics Committee of Guangzhou General Hospital of Guangzhou Military Command. Written informed consent was obtained from all participants.

PRP preparation. PRP were obtained using a two-stage centrifuging process. Whole blood samples (10 ml) were drawn from the participant's medial cubital vein and collected in a sterile tube containing 1 ml anticoagulant. Four tubes were collected per participant. After measuring the blood platelet concentration, the tubes were centrifuged at 1500 revolutions per minute (rpm) for 10 min in a centrifugal apparatus. The first spin separated platelet-poor plasma (PPP) from red blood cells (RBCs) and PRP. The PPP, PRP and a few RBCs were aspirated into a new tube, mixed, platelet concentration was detected again, and in the second spin, the tubes were centrifuged at 3000 rpm for 20 min. The upper section consisted of PPP and the PRP collected at the bottom of the tube. Then, 6-10 ml PPP and PRP were aspirated, mixed and platelet concentration was detected again to guarantee that the platelet concentration in the PRP ranged from 700,000,000-1,000,000,000 platelets per ml. Prior to treatment calcium gluconate was added at a ratio of 1:9 (calcium gluconate/plasma) to activate platelets.

Treatment. Prior to treatment, all treatment areas were gently cleansed using a mild cleanser, and a topical anesthetic cream was applied for 30 min. The entire face of each participant was then treated with an erbium fractional laser. Treatment parameters: wavelength, 2,940 nm; pulse duration, 300-600 μ sec; pulse energy, 600-1200 mJ (selected according to acne scar level); microbeam diameter, 2-7 mm; and penetration depth, 18-24 μ m. Concurrent forced-air cooling was used for the whole process. The end-point of the

laser treatment was moderate erythema or punctiform erythema (for severe acne scars). Following the treatment of the participants with autologous PRP, PRP mixed with calcium gluconate was coated onto each therapeutic area (thickness \sim 0.5 mm). Participants were then instructed to compress their faces with gauze for 15-20 min while remaining supine before being allowed to go home, and were instructed to avoid sun exposure. One or two months after the initial treatment, all participants underwent one additional treatment session with the same treatment.

Measurements. Photographic documentation was performed using identical camera settings and lighting and the same positioning with the same camera. After the first treatment session, participants were evaluated for adverse events at 7 days, 1, 2 and 3 months. Erythema and edema were graded on a 5-point scale (0, none; 1, trace; 2, mild; 3, moderate; 4, severe). Two dermatologists who were blinded to subject treatment group evaluated the serial photographs in a randomized fashion (before and after treatment, without labeling) to determine whether discernible clinical improvement had occurred. Evaluators used a quartile grading scale of 0 (no change, 0%), 1 (mild improvement, 0-25%), 2 (moderate improvement, 25-50%), 3 (marked improvement, 50-75%), and 4 (excellent improvement, 75-100%). In addition, each participant was asked to rate his/her overall satisfaction with the treatment 4 weeks after it was completed using a quartile grading system (0 unsatisfied, 1 slightly satisfied, 2 satisfied or 3 very satisfied). Patients were also asked to report on any side-effects of the treatment, including bleeding, oozing, post-treatment dyschromia, crust and duration of erythema.

Results

All 22 participants completed the study, and were followed up for 1-3 months. The serial photographs were evaluated prior to and following treatment (Figs. 1-4).

Erythema evaluation. All participants recorded the duration of erythema. The mean duration of erythema was 1.86 ± 0.87 days. In total, 95% of the erythema was moderate, only 1 patient who accepted laser grinding at a high pulse energy manifested severe erythema and 77% of the erythema lasted < 2 days.

Evaluation by dermatologists. On the quartile grading scale, the clinical improvement at 4 weeks after the first treatment was 2.77 ± 0.39 , corresponding to moderate improvement. A total of 68% of participants demonstrated excellent or marked improvement after the first treatment, while 90.9% demonstrated excellent or marked improvement after the third time. No patient was reported to show no improvement.

Self-evaluation. All participants showed satisfactory changes. According to the quartile grading scale, the self-evaluation was 3.3 ± 0.36 , and 91% of patients described themselves as 'satisfied' or 'very satisfied' with their overall improvement, and 45% wanted to receive further treatment.

Side-effects. Overall, the treatment was well tolerated. The patients felt apparent burning pain during the whole procedure

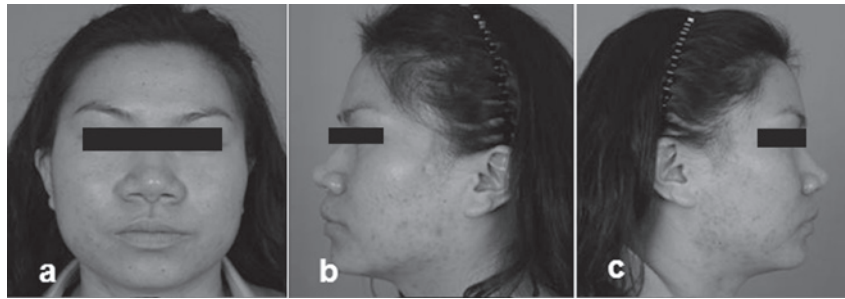


Figure 1. Development of clinical inflammation in the pilosebaceous unit (PSU) in a female. (a) Front, (b) lateral (right) and (c) lateral (left).

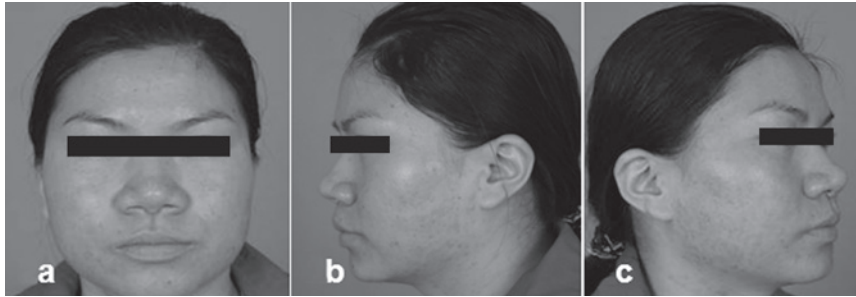


Figure 2. Platelet-rich plasma (PRP) combined with erbium fractional laser post-treatment 4 weeks. (a) Front, (b) lateral (right) and (c) lateral (left).

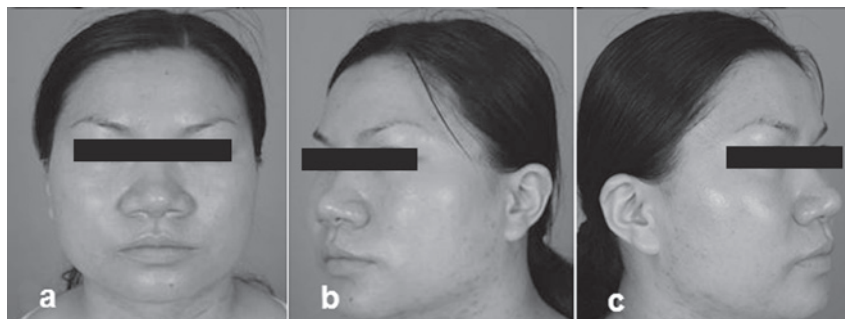


Figure 3. Platelet-rich plasma (PRP) combined with erbium fractional laser post-treatment 10 weeks. (a) Front, (b) lateral (right) and (c) lateral (left).

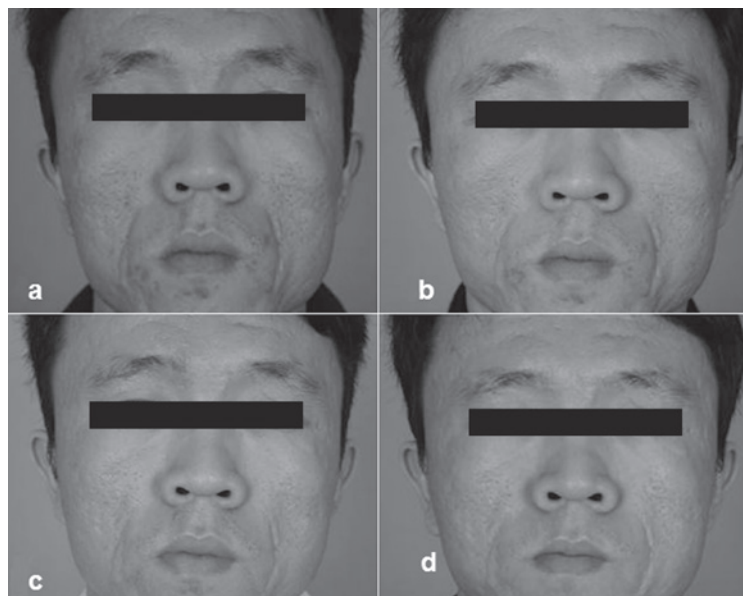


Figure 4. Severe acne scarring in a male (front). (a) Pre-treatment. Platelet-rich plasma (PRP) combined with erbium fractional laser post-treatment for (b) 4 weeks, (c) 12 weeks and (d) 20 weeks.

and some experienced punctiform erythema. Notably, after PRP was coated onto the face, the burning pain disappeared instead of tautness. Subsequently, at days 4 or 5 the epidermis of some patients desquamated, some formed a scab and the scab desquamated in 1 week. There were no participants with pigmentation.

Discussion

Acne has a prevalence of >90% among adolescents and persists into adulthood in ~12-14% of cases with psychological and social implications of high gravity (13). Types of acne scars include keloid, hypertrophic and atrophic scars (14). Atrophic acne scarring is by far the most common form, particularly on the face. A descriptive, universally acceptable classification system of atrophic acne scars includes three scar types: icepick, boxcar and rolling (15). Atrophic facial acne scarring is a widely prevalent condition that may negatively impact on a patient's quality of life (16). Acne scarring is common but difficult to treat. Treatments for acne scars include drugs, chemical peels, dermabrasion/microdermabrasion punch techniques, dermal grafting, needling, silicone gel combined therapy, intralesional steroid therapy, cryotherapy and pulsed dye laser surgery surgical ablation dermabrasion (16-19). Erbium fractional laser therapy is an effective treatment for facial acne scars. The 2,940-nm erbium fractional laser has the shortest duration of erythema, compared with other fractional lasers, which usually last for 3 days (17), and always resolves within 2 weeks. Moreover, there is a high probability of hyperpigmentation which usually lasts for ~1 month, and in rare cases up to 6 months; scar improvement is in the range of 26-83%; and the procedure may be relatively uncomfortable. Fractional laser skin resurfacing may cause adverse reactions such as erythema, acne, milia, infection, scarring and pigmentation (20). The complications of incomplete scar removal, poor intraoperative visualization, scar worsening, tissue fibrosis and permanent pigmentary alteration have limited the clinical utility of the treatment.

Autologous PRP is the plasma portion of autologously sourced blood with an iatrogenically high platelet concentration. At sites of tissue damage, platelets are the first cells to arrive and are important in mediating tissue repair through the release of growth factors from their α -granules. Platelet-derived factors may influence cellular growth, morphogenesis and differentiation and may be used therapeutically to accelerate the natural healing process (21). Studies have consistently shown that PRP concentrates are an abundant source of GFs; moreover, the proportion of these GFs approaches the human physiological ratio, therefore PRP concentrates are more effective than any single GF. PRP has wound-healing properties, affecting keratinocytes, endothelial cells, erythrocytes, fibroblasts and collagen. Hence, PRP may improve the quality of re-epithelialization and healing. Another study observed a greater proliferation of stem cells when the skin was treated with PRP activated with calcium and thrombin than with nonactivated PRP. To date, PRP has been confirmed to be useful for cosmetic and plastic surgery (22,23).

Kim *et al* used intradermal radiofrequency combined with autologous PRP in the treatment of striae distensae; it was administered to the participants once every 4 weeks.

The application of PRP not only accelerated recovery and reduced adverse events such as erythema or edema, but also enhanced localized collagen neogenesis and redistribution. All the participants showed satisfactory changes (24). Lee *et al* conducted a split-face trial that treated acne scars with PRP following ablative CO₂ fractional resurfacing. Fourteen Korean participants with acne scars were included in this study. They received one session of ablative CO₂ fractional resurfacing, and then facial halves were randomly assigned to receive treatment with autologous PRP injections on one side (experimental side) and normal saline injections on the other side (control side). Erythema edema on the experimental side improved faster than on the control side, and overall degree of clinical improvement was significantly better on the experimental side than on the control side (25).

All participants showed satisfactory changes in our study. According to the quartile grading scale, the self-evaluation was 3.3 ± 0.36 and 91% of patients described themselves as 'satisfied' or 'very satisfied' with their overall improvement, and 45% of participants wanted to receive the next treatment. On the quartile grading scale, the clinical improvement at 4 weeks after the first treatment was 2.77 ± 0.39 , corresponding to moderate improvement. A total of 68% of participants demonstrated excellent or marked improvement after the first treatment, while 90.9% demonstrated excellent or marked improvement after the third treatment. No patient was reported to show no improvement. The total duration of erythema lasted 1.86 ± 0.87 days on average. A total of 95% of the erythema was moderate, only one patient who accepted laser grinding at a high pulse energy manifested with severe erythema and 77% of the erythema lasted <2 days. All participants showed satisfactory changes, and no participants had pigmentation. Certain studies have demonstrated that PRP may also contain a small number of leukocytes that synthesize interleukins as part of a non-specific immune response (26). A previous study of PRP has demonstrated antimicrobial activity against *Escherichia coli*, *Staphylococcus aureus*, including methicillin-resistant *Staphylococcus aureus*, *Candida albicans* and *Cryptococcus neoformans*. In this study all the infected acne was cured, and in addition, after ablative erbium fractional resurfacing, no wounds were infected (27).

A combination of erbium fractional laser therapy and autologous PRP may have synergistic benefits on effectiveness and cause fewer adverse events. In our study, we did not compare the effects of erbium fractional laser therapy or autologous PRP alone with those of the erbium fractional laser and autologous PRP combination in the treatment of mild and moderate inflammatory acne and acne scars. PRP may be effective for controlling inflammation and promoting healing by inhibiting *P. acnes* and accelerating re-epithelialization and collagen remodeling. Further controlled studies are required to address such comparisons. Additionally, the optimization of treatment protocols and confirmation of the efficacy of treatment should be established by clinical trials involving larger numbers of patients.

Acknowledgements

This study was supported by the National Basic Science and Development Program of China (973 Program, 2012CB518105), the Major National Science and Technology Programs

(2011ZXJ09104-07C), the National Nature and Science Foundation of China (no. 81171812), the Guangdong Provincial Science and Technology Projects (nos. 2009B080701092 and 2011B061300073), and the Guangzhou City Science and Technology Project (10C36091671 and 2012J4100044).

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