Int J Clin Exp Med 2018;11(3):2654-2659
www.ijcem.com /ISSN:1940-5901/IJCEM0070728

*Original Article*

# Efficacy of autologous platelet-rich gel in the treatment of deep grade II burn wounds

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Received December 10, 2017; Accepted January 21, 2018; Epub March 15, 2018; Published March 30, 2018

**Abstract:** Objective: To analyze the clinical efficacy of autologous platelet-rich gel (APG) in the topical treatment of deep grade II burn wounds. Methods: Sixty-eight patients with deep grade II burn wounds were selected and divided into the treatment group and control group randomly and equally. The treatment group was treated with APG by wet application and the control group was treated with silvadene cream by external application. After one month of treatment, the differences between two groups were compared in healing time and ratio of healed area, the frequency of dressing changes, the positive rate of wound secretion bacterial culture and the scores of visual analogue scale (VAS). Besides, the levels of transforming growth factor β1 (TGFβ1) and epidermal growth factor (EGF) in burn wound tissues, the scar grades and the adverse reactions were also compared between two groups. Results: Compared to control group, the healing time, ratio of healed area, frequency of dressing changes, the positive rate of wound secretion bacterial culture of in treatment group were reduced (all $P<0.05$). In addition, the scores of VAS and Vancouver scar scale (VSS) in treatment group were lower than those in control group ($P<0.05$). However, there was no significant difference in the incidence of adverse reactions between two groups ($P>0.05$). The levels of TGFβ1 and EGF in burn wound tissue of treatment group were higher than those in control group ($P<0.05$). Conclusion: APG can effectively shorten the healing time, improve recovering rate, reduce frequency of dressing changes and the grade of wound pain, and then promote wound healing for patients with deep grade II burn wounds.

**Keywords:** Autologous platelet-rich gel, deep grade II burn, clinical efficiency, healing

## Introduction

The lesion damage of deep grade II burn wounds reaches dermis and can be further aggravated if infected. Therefore, the treatment principle of this kind of burn is to accelerate the wound healing [1]. The general measures used for wound treatment are dressing, changing dressings and performing skin grafting in post-treatment stage, however, the clinical practice confirmed their poor efficacy that wound healing was slow and wounds had scars. Besides, the tissue necrosis would further spread [2]. Therefore, it's important for clinical treatment to find more appropriate measures to accelerate wound healing. In recent years, the stem cell treatment, skin grafting and other methods have been applied to the treatment of deep grade II burn wounds and the therapeutic effects have been improved to some extent [3].

Reasonable and effective wound medication can accelerate wound healing [1]. The study on pathology proved that the wound repair is a very complicated process, which generally includes inflammatory reaction, tissue formation and wound shrinking and remodeling. The wound repair and regeneration mainly relies on the mutual intervention effects of inflammatory cells, growth factors and extra-cellular matrix and so on. During the process, growth factors (including TGFβ1, EGF, etc.) secreted by blood platelet are very important [4]. And the speed of wound healing might be accelerated by direct external application of the blood platelet concentrate containing rich growth factors on the topical wound [5].

The platelet rich plasma (PRP) is the platelet- and leucocyte-rich suspension which contains the growth factor mentioned above and is prepared by multiple centrifuges of autologous blood [6]. The autologous platelet-rich gel (APG), a kind of gelatinous substance, which is prepared by mixing up PRP, thrombin and calcification in proper proportion, has become a con-

cern and has been widely applied to the would treatment [7]. At present, however, the clinical effect of APG on patients with deep grade II burn wounds is still controversial in domestic. Therefore, this research aimed at analyzing the therapeutic effect of the APG on patients with deep grade II burn wounds.

## Materials and methods

### *Subjects of study*

This study had been approved by Ethics Committee and all the patients had signed informed consent forms. Sixty-eight patients with deep grade II burn who were treated in our hospital from January 2016 to December 2016 were selected. Deep grade II burn was consistently diagnosed by two senior attending physicians of burn surgery department, according to the criteria of "three grades with four types" method of burn depth. Inclusion criteria: patients aged less than 60; patients whose burns were all located in the trunk and limbs; patients who were naive to any wound treatments or treatments similar to APG. Exclusion criteria: patients who had significant dysfunctions in heart, brain, lung, kidney and other organ; patients who had severe complications and general infections and those who had poor general condition or were allergic to drugs they took.

### *Grouping*

According to random number table method, the patients were randomly separated into two groups, treatment group and control group, respectively. In treatment group, APG was directly applied to the wound by semi-exposed wet compressing. In control group, silvadene cream was applied to the wound by external compressing. Each group contained 34 cases.

### *APG gel preparation*

The APG was prepared according to the method proposed by Lv et al. and slightly revised [8]. First, 1 ml sodium citrate anticoagulation was added into a centrifuge tube and then 10 ml venous blood was extracted from patients. After mixing them up, centrifuged it at the speed of 1,500 rpm for 10 min and then extracted part of the plasma and red blood cells which was 1 mm close to the interface into another centrifuge tube. After centrifuging this tube at the speed of 3,600 rpm for 10 min, extracted out the upper plasma layer which contained a little amount of non-sedimentary blood platelets. The component of the rest plasma and blood cells was PRP. APG was made by mixing PRP with coagulant (1 ml calcium chloride and 1000U thrombin) in a 1 ml: 200U ratio. APG preparation should be completed in aseptic condition within 30 min.

### *Wound treatment method*

*Control group:* The wounds in patients were all thoroughly debrided with normal saline and 0.5% iodine, and all the decomposed skins were removed. Then, the wound was treated with 1% silvadene cream by external compressing and then covered with 10 layers of sterile gauze. The drug was changed every day until wound healing. Patients were given anti-infection, nutrition support and other symptomatic treatments.

*Treatment group:* Debridement measures were the same as those in control group. The APG treatment was in accordance with the method proposed by Wu et al. [9]. The APG was pasted on the wound and covered with 10 layers of sterile gauze. The external dressing was changed every 7 days until wound healing. At the same time, the anti-infection, nutrition support and other symptomatic treatment were given.

### *Follow-up and observation indexes*

*Wound healing indexes:* After one month of treatment, the differences in healing time, ratio of healed area, frequency of dressing changes of two groups was recorded and compared. The wound healing standard was 95% epithelization of wound, and it was consistently diagnosed by two senior attending physicians in burn surgery department. The ratio of healed area was calculated as follows: (the area of the healed surface/the initial wound area) *100%. On the 7th day of treatment, the secretions were collected from the wounds of patients in the two groups to perform bacterial culture, and the positive rate of wound bacterial culture was compared between them.

*Clinical efficacy indexes:* Wound pain: On the 7th day of treatment, Visual analogue scale (VAS) was used to assess pain grade [10]. Zero point meant painless and 10 points meant

**Table 1.** Comparison of basic data between the two groups

| Group | Age (year) | Sex ratio (male:female) | Diagnosis time (h) | Burn area (% body surface area) | Hypertension (%) | History of Diabetes (%) |
|---|---|---|---|---|---|---|
| Treatment group | 34.2±10.8 | 16:18 | 1.3±0.6 | 15.3±4.7 | 50.0 (17/34) | 35.3 (12/34) |
| Control group | 35.9±12.6 | 17:17 | 1.1±0.4 | 17.5±5.8 | 52.9 (18/34) | 32.4 (11/34) |
| $t/\chi^2$ | 0.597 | 5.735 | 1.617 | 1.718 | 6.115 | 6.412 |
| P | 0.552 | 0.098 | 0.111 | 0.090 | 0.089 | 0.062 |

**Table 2.** Comparison of wound healing between the two groups

| Group | Healing time (d) | Ratio of healed area (%) | Frequency of dressing changes | Positive rate of wound culture (%) |
|---|---|---|---|---|
| Control group | 20.7±6.6 | 77.1±10.4 | 19.1±3.8 | 38.2 (13/34) |
| Treatment group | 16.8±5.7 | 84.6±12.5 | 3.7±1.2 | 26.5 (9/34) |
| $t/\chi^2$ | 2.608 | 2.690 | 4.978 | 7.146 |
| P | 0.011 | 0.009 | 0.001 | 0.031 |

excruciatingly painful. Patients were asked to draw the corresponding point according to their own pain feelings.

Scar hyperplasia: All patients were followed up for 1 month after the wound healing, and Vancouver scar scale (VSS) was adopted to evaluate the scars, with the total score ranging from 0~15 points [11]. The higher the score, the worse the scar, and the lower the score, the lighter the scar.

Adverse reactions: All patients were followed up for 1 month after the wound healing, and the adverse reactions, including general malaise, increased pain and allergic eruption were recorded and compared between the two groups.

*Detection of growth factors in wound tissues:* The ulcer tissues in the wounds of patients in two groups were collected. After cutting up, the ultrasound homogenate was performed and the high-speed centrifugation was proceeded for 30 mins to separate the supernatants. The concentrations of transforming growth factor β1 (TGFβ1) and epidermal growth factor (EGF) in the supernatants were detected according to the instruction of ELISA Kit (purchased from American BD company) and the method of enzyme-linked immunosorbent assay (ELISA). Then, the differences were compared between the two groups.

*Statistical analysis*

Statistical analysis was performed with SPSS 17.0. Measurement data were expressed as mean ± standard deviation and analyzed with the pair t-test. Enumeration data were presented as rate and examined by chi-square test. $P<0.05$ indicated that differences were statistically significant.

## Results

*Comparison of basic data*

Thirty-three males and 35 females, with the average age of (35.4±11.2) years, were enrolled in the study. Burn area: 5-10% (36 cases), 11-20% (28 cases), above 20% (4 cases). The diagnosis time of wound (the period from the time when the burn was formed to the time of hospital admission) was 0.5-2 h, with the average time of (1.4±0.6) hours. There were no statistical differences in terms of age, sex ratio, diagnosis time, burn area, and past medical history ($P>0.05$, **Table 1**).

*Comparison of wound healing situation*

Compared with the control group, the treatment group exhibited shorter healing time, higher ratio of healed area, lower frequency of dressing changes and lower positive rate of bacterial culture ($P<0.05$, **Table 2**).

*Comparison of indicators of clinical efficacy*

The scores of VAS and VSS in the treatment group were significantly lower than those in the control group ($P<0.05$). There was no significant difference in the incidence of adverse reactions between the two groups ($P>0.05$, **Table 3**).

**Table 3.** Comparison of indicators of clinical efficacy between the two groups

| Group | VAS score | VSS score | General malaise (%) | Increased pain (%) | Allergic eruption (%) |
|---|---|---|---|---|---|
| Control group | 7.1±1.3 | 9.0±0.6 | 5.9 (2/34) | 23.5 (8/34) | 8.8 (3/34) |
| Treatment group | 5.9±1.7 | 8.4±1.1 | 5.9 (2/34) | 20.6 (7/34) | 5.9 (2/34) |
| $t/\chi^2$ | 3.269 | 2.792 | | 6.286 | 6.783 |
| P | 0.002 | 0.007 | | 0.076 | 0.059 |

Note: VAS, visual analogue scale; VSS, Vancouver scar scale.

**Table 4.** Comparison of indexes of curative effects between the two groups

| Groups | TGFβ1 (ng/ml) | EGF (ng/ml) |
|---|---|---|
| Control group | 23.7±7.6 | 14.1±5.4 |
| Treatment group | 30.8±9.8 | 18.2±6.3 |
| t | 3.338 | 2.881 |
| P | 0.001 | 0.005 |

Note: EGF, epidermal growth factor.

*Comparison of levels of growth factors in wound tissues*

The levels of TGFβ1 and EGF in wound tissues of the treatment group were significantly higher than those in the control group ($P<0.05$, **Table 4**).

## Discussion

The wound healing results of deep grade II burn are closely related to timely clinical intervention. Clinical practice has confirmed that improper wound disposals can induce infection easily, which can delay wound healing or even deepen it and scar hyperplasia is comparatively serious even though the wound is healed. Therefore, searching for more appropriate treatments for speeding up the wound healing in clinical treatment are urgent. In recent years, stem cell therapy, skin grafting and other treatment methods have been used in clinical treatment of deep grade II burn and the curative effects has been improved to some extent [3]. The previous study also confirmed that PRP has a good clinical efficacy in the treatment of diabetic ischemic ulcers, pressure ulcers and refractory wound of lower limb fracture [12]. Therefore, in this study, the APG was applied to the treatment of deep grade II burn wounds on the basis of traditional treatment measures. The results showed a good clinical efficacy.

In this study, APG was used to treat patients with deep grade II burn wounds, with the external application of silvadene cream as a control. The results showed that the wound healing time, the ratio of healed area and the frequency of dressing changes in treatment group were significantly lower than those in control group, indicating that APG, obviously, had better clinical effect on wound healing. The possible reasons might be as follows. First, PRP contains a variety of growth factors and fibrin proteins in high concentration, which can effectively compensate for the low level of growth factors in wounds, speed up the initiation of repair mechanisms and provide a better micro-environment for wound repairing [13]. Second, there is a large number of white blood cells and mononuclear cells in PRP, which can facilitate the anti-infection of wound, inhibit the proliferation of staphylococcus aureus, and the expansion of the injury area effectively. It can be confirmed by the lower positive rate of wound bacterial culture in the treatment group [14]. Third, PRP can reduce wound exudative swelling, stimulate blood vessel regeneration and reduce the pain of wound [15]. Fourth, recent studies have also confirmed that the concentration and proportion of diverse growth factors in autologous PRP are similar to the physiological level in body, which can ensure the better coordination of growth factors, the inflammation immune balance and avoid the occurrence of immunological rejections [16]. Fifth, PRP has good effect on increasing collagen deposition and early wound strength, accelerating wound soft tissue repair, and wound epidermidalization growth [17, 18]. On the 7th day of treatment in this study, the VAS scores of patients in treatment group was significantly lower than that in control group, indicating that APG had obvious better effect on alleviating the pain. At the first month after healing, the VSS scores of treatment group was significantly lower, suggesting that patients had better wound healing and unapparent scar hyperplasia. It may be associated with the good tissue adhesion of APG which can prevent platelet from losing and

maintain the high concentration of growth factors and shrink the wound and so on [19, 20]. Further analysis showed that the levels of TGFβ1 and EGF in the wound tissues of the treatment group were significantly higher than those in the control group, which may also be one of the main reasons for APG to promote wound healing. This result was consistent with previous studies.

What is noteworthy is that the application of APG does not increase the occurrence of various adverse reactions, suggesting that it has preferable security in clinical practice. However, there still are some shortcomings of APG in the process of clinical application. For example, APG is easy to be polluted in the preparation process and the platelets are susceptible to over-activation triggered by exogenous stimulation and then it can reduce the level of growth factors. Therefore, medical staff should complete the preparation in aseptic condition within 30 min.

In conclusion, the application of APG in deep grade II burn wounds could effectively improve the concentration of local growth factors, shorten the healing time and increase the healing rate. Meanwhile, it has good security. Therefore, APG is suitable for clinical application.

## Disclosure of conflict of interest

None.

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